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Articoli originali

Original articles

Tuberculosis deaths in a tertiary hospital in Goiânia, Brazil: a descriptive study

Studio descrittivo della mortalità per tubercolosi in un ospedale terziario in Goiânia, Brasile

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INTRODUCTION

Tuberculosis (TB) is a major infectious disease that affects humans. Currently, it is estimated that one third of the world population is infected with *Mycobacterium tuberculosis* (Mtb), which is the main etiological agent of tuberculosis. In Brazil, TB is distributed throughout the country with an incidence rate of 37.9 per 100,000 inhabitants [1]. In Goiás, 830 new TB cases were reported in 2008. In 2009, 875 new cases of TB were reported in the state of Goiás, with an incidence of 14.8 cases per 100,000 inhabitants and a mortality rate of 2.5 deaths per 100,000 inhabitants. Goiânia and Aparecida de Goiânia exhibited a higher number of cases. The Municipality of Goiânia reported 195 new cases of TB in 2008, 246 in 2009, and 243 in 2010 [2]. Brazil presents several TB epidemiological realities. The State of Goiás has the lowest incidence rate (14.8), contrasting for example with the Rio de Janeiro State where in 2011 the incidence was 70.7 new cases per 100.000 inhabitants. Some aspects could be correlated with this lower TB incidence rate such as a better socioeconomics income of the State of Goiás, lower population densities, and different climate among others [3].

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TB, when properly treated, has a cure rate greater than 90%. Nowadays TB is treated following the Brazilian Health Ministry, which recommend two treatment regimens. Basic treatment that is suitable for all types of TB, except CNS involved case, the treatment is composed of rifampicin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E), with a treatment duration of 6 months. TB treatment in the CNS uses the same drugs as in the basic scheme, with an increase in treatment duration to 9 months [4]. TB treatment is currently performed in outpatient services, with hospitalization recommended for more severe cases or cases with social problems [5]. Hospitalization is recommended by the Brazilian National Tuberculosis Control for special cases, based on the following priorities: meningoencephalitis; surgical indications of because of tuberculosis because of severe complications of tuberculosis or comorbidities; uncontrollable outpatient drug intolerance; clinical complications and/or surgical injury; an overall state that does not allow treatment on an outpatient basis, which in social cases, includes a lack of a fixed home or groups most likely to dropout, especially if it is a case of bankruptcy or retreatment [5, 6]. However, even in its severe forms, TB is considered a treatable disease which raises the question as to why it is the third leading cause of death among infectious diseases and the first among individuals with acquired immunodeficiency syndrome (AIDS).

Mortality statistics are frequently based only on the underlying cause of death, as described in death certificate (DC) [7]. However, the introduction of an analysis by multiple causes, which includes both immediate causes and associated diseases, can bring significant gains to the study of some diseases or conditions that are not usually mentioned on the death certificate.

Given the high mortality rate of TB, it is of great importance to characterize patients with TB who died so that target populations can be identified to implement specific measures to reduce mortality. The objective of this study was to calculate the mortality of TB patients and describe their clinical, laboratory and radiology characteristics. All patients examined in this study died at the Tropical Diseases Hospital in Goiânia, between January 2008 and December 2009.

MATERIALS AND METHODS

Study Design

This was a retrospective descriptive study.

Population and study site

The study population consisted of 39 patients, who died with TB that were diagnosed and reported during the period January 1st 2008 to December 31st 2009, while being treated at the Tropical Diseases Hospital Dr. Anuar Auad (HDT).

The HDT is a state public institution in Goiás that is part of the Unified Health System; patients are referred to this hospital for the treatment of infectious diseases, including patients with TB who require hospitalization.

Eligibility and exclusion of cases

Eligible cases were patients with that meet the following criteria: diagnosis of active pulmonary and/or extrapulmonary TB based on clinical criteria, radiological and/or laboratory criteria, positive smear and/or culture, or judgment of the attending physician to initiate treatment for tuberculosis. Inclusion criteria for infection by human immunodeficiency virus (HIV/AIDS) were in accordance with those adopted by the Ministry of Health [7]. Exclusion criteria were being younger than 18 years old, being pregnant, lactating, being of an indigenous status and having an incomplete medical chart.

All patients with TB who died before completing the treatment were considered in this study [8].

Immediate causes of deaths recorded in death certificates as cardiopulmonary arrest (CPA) or as multiple organ failure were analyzed as causes not defined [9].

Information source

Uniquely identified patients in the surveillance system and the medical archive of HDT/HAA, had their medical records and death certificates reviewed for data collection, and the results were recorded using a specific data recording system.

The following clinical data were transcribed: age, sex, weight, cough, fever, weight loss, dyspnea, and diarrhea. The following laboratory data were transcribed: haemoglobin, haematocrit and albumin.

The following additional information was also transcribed: clinical forms of the disease, pulmonary radiological findings, tuberculin skin test (TT), research alcohol acid bacillus (AFB) in sputum [or other biological sample: cerebrospinal fluid (CSF), pleural fluid and urine], culture, albumin and haemoglobin, haematocrit, total leukocyte counts, TB treatment and continuity of care until death, and associated diseases. The underlying and immediate causes were also recorded based on data from the death certificates.

Values

Anemia was assessed by haemoglobin (Hb) and haematocrit (Ht) levels in the blood. The criteria used in this study were as follows: anemia was defined as Hb <10 g/dL and/or Ht <41%; severe anemia was defined as Hb <7 g/dL and/or Ht <25% [10].

Nutritional assessment in this study was based on biochemical parameters of serum albumin levels. The following albumin concentrations were used in this study: moderate nutritional depletion was defined as <3.5 g/dL, and severe nutritional depletion was defined as <2.4 g/dL [11].

Statistical analysis

The collected data were tabulated in Excel 2010 version. The statistical analysis was conducted using EpiInfo® version 3.5.3 (CDC, Atlanta, Georgia). Frequencies were determined for categorical variables, and medians, means and standard deviations for continuous variables.

Ethical issues

The study was approved by the local Ethic Committee (Institutional Review Board-equivalent) and was conducted in accordance with the provisions of the Declaration of Helsinki (protocol CEP/HDT - 036/2010).

RESULTS

There were 283 diagnosed and reported cases of TB at the HDT/HAA between 2008 and 2009, and 39 recorded deaths occurred, resulting in a lethality index of 14%. Among these deaths, men accounted for 82%.

Of the patients who died, 82% were aged 18-39 years, with a mean age of 42 years and a median age of 37 years.

Pulmonary TB was the most common form of TB detected in this study at 51.3% of the patients, and the second most common type was disseminated TB at 30.8% of the patients. Among the clinical signs evaluated until the date of diagnosis of the disease, 69.2% of patients had a cough for more than three weeks, 79.5% of the patients experienced weight loss, 74.4% of the patients experienced fever for more than three weeks, and dyspnea was observed in 59% of patients (Table 1).

A culture of acid-fast bacilli (AFB) in the sputum was requested in 92% of the cases, and 78% of these cases were positive.

An examination of the sputum culture or other biological material, such as pleural fluid, cerebrospinal fluid (CSF), urine, were required in 23 patients, showing a positivity rate of 17.4% of the cases. Of the eight patients who underwent tuberculin test (TT), 50% had positive results (Table 2).

A chest radiograph was available for analysis in 75% (n=30) of patients. The occurrence of bilateral infiltrates (n=19) includes the following: miliary pulmonary disease (n=9), interstitial lung disease (n=6) and non-cavitary bilateral pulmonary disease (n=4). The presence of cavitation was less frequent and was detected in only one case (Table 3).

Laboratory evaluation was performed for albumin, haematocrit, haemoglobin and leukocytes. The albumin was tested in 23 patients, 19 patients had concentrations lower than 3.5 g/dL and 4 patients had concentrations above 3.5 g/dL.

We established a critical concentration of albumin at a value less than 2.4 g/dL. Of the 19 patients who had albumin less than 3.5 g/L, 15 patients had albumin values of less than 2.4 g/dL (Table 4).

Table 1 - Clinical characteristics of patients who died from tuberculosis in the Hospital for Tropical Diseases, State of Goiás, Brazil - 2008/2009.

		Patients (n=39)
Age (years), n/%	18-39	20/51.3%
	40-59	13/33.3%
	>60	6/15.4%
Gender, n/%	Female	7/18%
	Male	32/82%
Clinical forms of TB, n/%	Pulmonary	20/51.3%
	Disseminated	12/30.8%
	Pleuropulmonary	3/7.7%
	Central nervous system	3/7.7%
	Lymph node	1/2.5%
Signs and symptoms, n/%	Fever >3 weeks	29/74.4%
	Cough >3 weeks	27/69.2%
	Weight loss	31/79.5%
	Diarrhea	11/28.2%
	Dyspnea	23/59%
Coinfection TB/HIV, n/%	Coinfected TB/HIV	22/56.4%
	Non-coinfected TB/HIV	17/43.6%

TB = tuberculosis; HIV = Human Immunodeficiency Virus.

Table 2 - Acid-fast bacilli sputum smear, tuberculin skin test and *Mycobacterium tuberculosis* culture findings in cases of deaths by tuberculosis in the Tropical Diseases Hospital, State of Goiás, Brazil - 2008/2009.

Tests	*Patients (n=39)*
Acid-fast bacilli sputum smear, n/%	
Positive	28/71.8%
Negative	8/20.5%
Unknown/not done	3/7.7%
Tuberculin Skin Test	
Positive	4/10.2%
Negative	4/10.2%
Unknown/not done	31/79.6%
***M. tuberculosis* culture, n/%**	
Positive	4/10.2%
Negative	19/48.7%
Unknown/not done	16/41%

Table 3 - Radiological findings in cases of deaths by tuberculosis in the Tropical Diseases Hospital, State of Goiás, Brazil - 2008/2009.

Chest radiography	*Patients, n/%*
Unilateral infiltrate	2/5.1%
Cavitation	1/2.6%
Pleural effusion	3/7.7%
Normal	5/12.8%
Bilateral infiltrate	19/48.7%
Unknown/not done	9/23.1%

Table 4 - Laboratory characteristics in cases of deaths by tuberculosis in the Tropical Diseases Hospital, State of Goiás, Brazil - 2008/2009.

	Patients (n)
Albumin (g/dL)	
<3,5	19
>3,5	4
Albumin (g/dL)	
<2,4	15
>2,4	8
Haematocrit (%)	
<41	34
>41	4
Haematocrit (%)	
<25	9
>25	29
Haemoglobin (g/dL)	
<10	25
>10	13
Haemoglobin (g/dL)	
<7	10
>7	28

Thirty-eight patients had their haematocrit concentrations evaluated. Four patients had haematocrit values greater than 41% and 34 patients had haematocrit values less than 41%. Of the patients with haematocrit values less than 41%, nine had a haematocrit less than 25%. Haemoglobin concentrations was determined in 38 patients, of these 25 patients had a value less than 10 g/dL, and 10 cases were less than 7 g/dl (Table 4).

The underlying causes of death, as reported in the DC, were analyzed, with 67.3% of the patients dying from TB and 33.7% of the patients dying from TB/AIDS co-infections. We analyzed the immediate causes of deaths recorded in the DC, which included the following: sepsis (n=8), acute respiratory failure (ARF) (n=12), brain death (n=1), neurogenic shock (n=1), cardiogenic shock (n=1), acute lung edema (n=1), hepatic insufficiency (n=1), and ignored or undefined causes (n=14) (Table 5).

Of the 39 TB patients who died, 56.4% (n=22) were co-infected with HIV.

Among the 39 patients who died, 11 had HIV associated diseases: neurotoxoplasmosis (n=3), *Pneumocystis jiroveci* pneumonia (n=7), histoplasmosis (n=1) (Table 6).

This study identified smoking and alcohol consumption in 17 and 14 of the patients who died from TB, respectively.

Twenty-nine patients were admitted to the ICU; of these 16 were HIV+. Mechanical ventilation (MV) was used in 27 patients, 14 were HIV+ and 13 were HIV-. The average length of stay of these patients in the ICU was 7.3 days, and the mean hospital stay was 13.7 days.

Table 5 - Immediate causes deaths recorded in the death certificated in cases of deaths by tuberculosis in the Tropical Diseases Hospital, State of Goiás, Brazil - 2008/2009.

Immediate causes	*Patients (n=39) (%)*
Sepsis	8 (20%)
Acute Respiratory Failure	12 (30%)
Brain Death	1 (2.5%)
Neurogenic shock	1 (2.5%)
Cardiogenic shock	1 (2.5%)
Acute lung edema	1 (2.5%)
Hepatic insufficiency	1 (2.5%)
Unknown	14 (35%)

Table 6 - Diseases associated with patients in cases of deaths by tuberculosis and HIV/AIDS in the Tropical Diseases Hospital, State of Goiás, Brazil - 2008/2009.

Diseases associated	*Patients HIV+ (n)*
Histoplasmosis	1
Neurotoxoplasmosis	3
Pneumocystis jiroveci pneumonia	7
Total	11

Thirty-four patients had not been treated for TB prior to admission to HDT/HAA and were characterized as newly diagnosed cases who were receiving a basic treatment and 3 patients received TB treatment in the CNS.

DISCUSSION

In this study, the mortality rate was 14% at HDT/HAA from 2008 to 2009. This mortality rate was below what Galesi et al. observed in São Paulo hospitals (30.6%) [5].

Although the present study's mortality rate appears low when compared to the Galesi et al. study, the mortality rate of 14% is high when compared to other highly lethal acute diseases, such as meningococcal meningitis (approximately 18% and 16%, respectively) and leptospirosis (approximately 13% and 10%, respectively) as studied in the State of Goiás in 2008 and 2009 [12].

The lethality of TB in our institution was approximately 2 times higher than the fatality rate for all forms of TB in Brazil and Goiás during the same time period. In Brazil, the mortality rate was 6.9% in 2008 and 6.5% in 2009. In Goiás, the mortality rate for TB was 6.4% in 2008 and 6.2% in 2009 [13].

HDT is a tertiary hospital for treatment of infectious diseases that includes serious and complex TB patients, which would explain the higher mortality rate at HDT.

Among the patients who died from TB, 32 (82%) were men. Oliveira et. al. noted the predominance of males (71.3%) among patients with TB/HIV+ and TB/HIV- who died during 1996-2003 in the city of Campinas, São Paulo [14]. The predominance of male TB cases can be explained by greater exposure of men to the disease, a product of male's own behavioral characteristics and/or greater difficulty in treatment observance.

Of the 39 patients with TB who died in this study, 22 (56.4%) were HIV+. Lins et al. retrospective cohort study found that HIV infection was a risk factor for death among patients with TB [15]. Oliveira et. al. study showed that male subjects, aged 30-39 years that are co-infected with HIV had a higher mortality [14]. These findings are similar to what is observed in this study, wherein the age group with the highest mortality rate was between 18-39 years of age (n=20), of these 20 cases 15 presented with HIV co-infection. It is valid to note that most patients with TB are employed and the majority is between the ages of 30-39 years [16].

The most frequent clinical form among out study population was pulmonary TB at 51.3% (n=20) and the second most frequent was disseminated TB at 30.8% (n=12). The disseminated form of TB affected more AIDS patients (n=9) than HIV- (n=3), which is similar to the work of Klautau & Kuschnaroff that found that a higher proportion of deaths among patients with disseminated TB were co-infected with HIV [17].

The Information System Diseases Notification data for Goiás shows a higher prevalence of pulmonary TB than what was observed in this study, with 80.9% of cases in 2008 and 82.8% of cases in 2009 [13]. The high frequency of disseminated TB in our study is most likely due to the severity of the patients and the high occurrence of coinfected with HIV (56.4%).

The frequency of patients with symptoms such as cough, fever, weight loss, dyspnea and diarrhea until the date of diagnosis of the disease more than 3 weeks were 74.4%, 69.2%, 79.5%, 59%, and 33.3%, respectively. There are some differences in the symptoms of TB between HIV+ and HIV- patients. The most common symptoms in HIV+ TB patients are fever (88%), weight loss (79%) and cough (59%) within the least six weeks. According Cain et al. the presence of at least three symptoms was more sensitive for the diagnosis of tuberculosis among HIV+ patients than just cough for more than three weeks. In this study, cough for more than three weeks was used as a diagnostic criterion that detected approximately 50% of TB cases in HIV- positive. The most common symptoms that could be part of a diagnostic algorithm are the following: cough of any duration, fever of any duration, night sweats for more than three weeks or loss of appetite any time in the last four weeks [18].

The AFB was performed in 36 patients, with positive results observed in 28 cases. Culture of sputum or other biological material was made in 23 patients, with 7 positive results. These results were similar to those observed in studies of Clevenbergh et al. and Lins et al., wherein most requested AFB of TB patients showed high positivity [15, 19]. This result can be explained by medical criteria adopted by requesting routinely AFB, in view of the symptoms of patients admitted to the HDT/HAA.

Bilateral pulmonary disease was the most frequent radiological presentation of TB patients

who died (48.7%). These findings were similar to Lins et al., in which 51.8% of TB patients with HIV+ and HIV- had the same radiographic findings [15].
Additionally, in this study 12.8% of TB patients showed no radiographic changes. Because, both HAA and HDT receives patients with severe TB for hospitalization and/or treatment of complications the typical pattern of unilateral upper lobe infiltrate is uncommon in the study's TB group. Cavitary pulmonary disease was found in only one patient, whom was co-infected with HIV.
Twenty-five patients had haemoglobin concentrations less than 10 g/dL, 10 of these cases showed less than 8 g/dL, and 13 patients had haemoglobin greater than 10 g/dL. In evaluating the haematocrit, 34 patients had a value less than 41% with a subset of nine patients that had a value less than 25%. In Mugusi et al. study low haemoglobin was associated with mortality in patients with TB [20]. In a study by Van Rie A. et al., anemia was a risk factor for TB co-infected HIV+ patients who started treatment for TB [21].
Twenty-three patients had evaluated albumin levels; 19 patients were less than 3.5 g/dL, 15 patients were less than 2.4 g/dL. These albumin levels suggest a state of malnutrition of patients coming to HDT/HAA; additionally, chronic disease is a cause of malnutrition that can worsen the nutritional status of the patient [20].
The assessment of the nutritional status of patients in this study was limited by lack of data on their medical charts. The Brazilian study by Chiavegatto-Filho et al., found that malnutrition was an underlying or associated cause of death among women aged 10 to 49 years who were infected with TB, these women died while residing in the States capitals or the Federal District [22].
These four factors were associated with the prevalence of disseminated TB, and it was observed that a score of high nutritional risk was a good predictor of poor outcome to treatment for patients with disseminated TB [23].
Among the immediate causes of death sepsis (n=8) and ARF (n=12) were the most frequent. A study conducted by Santo et al. examined a group of 1,644 patients that had a reported primary cause of death as TB; their main immediate causes of deaths were respiratory failure (46.9%), pneumonia (16.5%), other specified symptoms and signs related to circulatory and respiratory (13.9%), and septicemia (7.2%) [24].
The deaths in which tuberculosis was mentioned as an associated cause had the main underlying cause of AIDS (65.3%), which is higher than the present study that had a primary cause attributed to AIDS at 33.3%.
Most likely, the immediate cause of death may not match the actual causes of death because of inconsistency in completing the death certificate of the patients and the absence of performing autopsies on patients who died in this unit.
Amancio et al. found that among the 125 AIDS patients admitted to the ICU respiratory failure was the leading cause of admission (43.2%); followed by neurological disorders (24.8%), sepsis (20%), heart failure (1.6%) and other (10.4%). The ICU and hospital mortality rates were 46.4% and 68%, respectively [25].
The mortality rate in the ICU and hospital study by Amancio et al. was similar compared to the present study with mortality rates of 69% and 31%, respectively. Silva et al. found that comorbidities especially those related to immunosuppression, such as HIV infection, are considered risk factors for progression to respiratory failure, and these patients will require MV [26].
Among patients who died of TB, 43.6% were smokers and 36% were drinkers. In a study by Lindoso et. al. found that of 416 patients with TB, who died during the study, 71% were smokers and 64% were alcoholic [27]. However, in the study by Silva et al. tobacco and alcohol use was not considered a risk factor for death among TB patients in this study [26].

CONCLUSION

This study found that hospitalized patients who died had the following characteristics: bilateral pulmonary disease, low levels of haemoglobin and haematocrit, albumin, and those co-infected with HIV that has been admitted to the ICU required MV.
Educational efforts should be made in this health unit for more complete medical records, for a proper completion of death certificates, and autopsy in cases with no defined cause of death.
Prospective studies aiming to analyze the risk factors for death from TB are needed to better understand this process.

Keywords: Tuberculosis, death causes, lethality, descriptive study.

SUMMARY

Tuberculosis (TB) remains a serious global public health problem, being the main cause of death in patients with AIDS, and the third cause of death by infectious diseases throughout the world. This is somewhat surprising because TB is a disease that, if treated properly, displays high rates of healing. It is therefore important to characterise these patients to identify target populations for specific measures seeking to reduce TB deaths. We performed a retrospective descriptive study to analyse the cases of TB deaths in a State public hospital, a point of reference for treatment of infectious diseases, located in the Central-West region of Brazil, in the period from January 1st, 2008 to December 31st, 2009. There were 283 diagnosed and reported cases of TB between 2008 and 2009, and 39 recorded deaths occurred, resulting in a lethality index of 14%. The mean age of TB patients was 42 years, and the median age 37 years. Pulmonary TB was the most common form of TB (51.3% of the patients). Of the 39 TB patients who died, 56.4% (n=22) were co-infected with HIV. The main immediate causes of death were acute respiratory failure (n=12) and sepsis (n=8). Anaemia and hypoalbuminaemia were prevalent in this group, and 27 patients required mechanical ventilation. This study found that hospitalized patients who died had the following characteristics: bilateral pulmonary disease, low levels of haemoglobin and haematocrit, albumin, and those co-infected with HIV that were admitted to the ICU required MV. Prospective studies aiming to analyse the risk factors for death from TB are needed to better understand this process.

RIASSUNTO

La tubercolosi (TB) costituisce ancora oggi un problema di salute pubblica globale, essendo la principale causa di mortalità nei pazienti affetti da AIDS e la terza causa di morte per malattie infettive in tutto il mondo. Questi dati epidemiologici sono sorprendenti in considerazione del fatto che, se trattata correttamente, i tassi di guarigione di questa sono elevati. È pertanto importante caratterizzare questi pazienti per identificare le popolazioni bersaglio da sottoporre a misure specifiche tese a ridurre i decessi per TB. Abbiamo effettuato uno studio descrittivo, retrospettivo, per analizzare i casi di decessi per TB in un ospedale pubblico, di riferimento per il trattamento delle malattie infettive, situato nella regione centro-occidentale del Brasile, nel periodo 1° gennaio 2008 - 31 dicembre 2009. I casi di TB diagnosticati e segnalati nel periodo studiato ammontavano a 283 e i decessi a 39, con un indice di letalità del 14%. L'età media dei pazienti con TB era di 42 anni, l'età mediana di 37 anni. Delle diverse forme di TB, quella polmonare era la più comune (51,3% dei pazienti). Ventidue (56,4%) dei 39 pazienti con TB deceduti erano coinfettati da HIV; le principali cause di decesso improvviso sono risultate l'insufficienza respiratoria acuta (n=12) e la sepsi (n=8). In questo gruppo di pazienti anemia e ipoalbuminemia erano prevalenti e per 27 pazienti si era resa necessaria la ventilazione meccanica.

Questo studio ha riscontrato che i pazienti deceduti presentavano le seguenti caratteristiche: malattia polmonare bilaterale, bassi livelli di emoglobina, dell'ematocrito e di albumina. Inoltre, i pazienti con coinfezione da HIV ricoverati in Unità di Terapia Intensiva necessitavano di ventilazione meccanica. Per una migliore comprensione di questo processo sono necessari studi prospettici tesi ad analizzare i fattori di rischio di mortalità per TB.

REFERENCES

[1] World Health Organization 2010. Report 2010. Global tuberculosis control 2010. WHO, Geneva.

[2] Secretaria Estadual de Saúde 2011. http://www.saude.go.gov.br Last accessed December 20, 2011.

[3] Ministério da Saúde. Sistema nacional de vigilância em saúde: relatório de situação: Goiás/Ministério da Saúde, Secretaria de Vigilância em Saúde. - 5th ed. - Brasília, 2011.

[4] Ministério da Saúde. Secretaria de Vigilância em Saúde, Departamento de Vigilância Epidemiológica. Manual de Recomendações para o Controle da Tuberculose no Brasil, Brasília, 2011.

[5] Galesi V.M.N., Almeida M.M.M.B. Indicadores de morbimortalidade hospitalar de tuberculose no Município de São Paulo. *Rev. Bras. Epidemiol.* 1, 48-55, 2007.

[6] Ribeiro S.A., Matsui T.N. Hospitalização por Tuberculose em Hospital Universitário. *J. Pneumol*. 29, 9-14, 2003.

[7] Ministério da Saúde. Secretaria de Vigilância em Saúde. Programa Nacional de DST e Aids. Critérios de definição de casos de aids em adultos e crianças. Ministério da Saúde, Secretaria de Vigilância em Saúde, Programa Nacional de DST e Aids. Brasília, 2004.

[8] World Health Organization. Treatment of tuberculosis Guidelines, 4th ed., Geneva, 2010.

[9] Ministério da Saúde. A declaração de Óbito: documento necessário e importante. 3th ed, Brasília, 2009.
[10] Foster C., Mistry N.F., Peddi P.F., Sharma S. The Washington Manual of Medical Therapeutics. LWW. 33th ed. Washington. 2011.
[11] Cuppari L. Nutrição Clínica no Adulto - Guia de Medicina Ambulatorial e Hospitalar da UNIFESP - *EPM*. Manole. 2nd ed. São Paulo, 2010.
[12] Ministério da Saúde. Sistema nacional de vigilância em saúde: relatório de situação: Goiás/Ministério da Saúde, Secretaria de Vigilância em Saúde. - 5th ed. - Brasília, 2011.
[13] SINAN, Sistema de Notificação de Agravos de Notificação, http://dtr2004.saude.gov.br/sinanweb/tabnet/dh?sinannet/tuberculose/bases/tubercbrnet.def last accessed November 20, 2012.
[14] Oliveira H.B., Marín-León L., Cardoso J.C. Perfil de mortalidade de pacientes com tuberculose relacionada à comorbidade tuberculose-Aids. *Rev. Saúd. Públic.* 38, 503-510, 2004.
[15] Lins T.B.A., Soares E.M., Santos F.M., Mandacaru P.M.P., Pina T., Araújo-Filho J.A**.** *Mycobacterium tuberculosis* and human imumnodeficiency virus coinfection in a tertiary care hospital in Midwestern Brazil. *Infez. Med.* 20, 108-116, 2012.
[16] Nakanjako D., Mayanja-Kizza H., Ouma J., et al. Tuberculosis and human immunodeficiency virus co-infections and their predictors at a hospital based HIV/AIDS clinic in Uganda. *Int. J. Tuberc. Lung Dis.* 14, 1621-1628, 2010.
[17] Klautau G.B., Kuschnaroff T.M. Clinical forms and outcome of tuberculosis in HIV infected patients in a tertiary hospital in Sao Paulo - Brazil. *Braz. J. Infect. Dis*. 9, 464-478, 2005.
[18] Cain K.P., McCarthy K.D., Heilig C.M., et al. 2010. An algorithm for tuberculosis screening and diagnosis in people with HIV. *N. Engl. J. Med.* 362: 707-716.
[19] Clevenbergh P., Maitrepierre I., Simoneau G., et al. Lymph node tuberculosis in patients from regions with varying burdens of tuberculosis and human immunodeficiency virus (HIV) infection. *Presse Med*. 39, 223-230, 2010.
[20] Mugusi F.M., Mehta S., Villamor E., et al. Factors associated with mortality in HIV-infected and uninfected patients with pulmonary tuberculosis. *BMC Public Health* 9, 409, 2009.
[21] Van Rie A., Westreich D., Sanne I. Tuberculosis in patients receiving antiretroviral treatment: incidence, risk factors, and prevention strategies. *J. Acquir. Immune Defic. Syndr*. 56, 349-355, 2011.
[22] Chiavetto-Filho A.D.P., Laurenti R., Gotlieb S.L.D., Jorge M.H.P.M. Desnutrição como causa básica ou associada de morte: análise da qualidade de informação em mulheres em idade fértil. *Rev. Bras. Epidemiol.* 1, 30-38, 2007.
[23] Kim D.K., Kim H.J., Kwon H.Y., et al. Nutritional deficit as a negative prognostic factor in patients with miliary tuberculosis. *Eur. Respir. J.* 32, 1031-1036, 2008.
[24] Santo A.H., Pinheiro C.E., Jordani M.S. Causas múltiplas de morte relacionadas à tuberculose no Estado de São Paulo, 1998. *Rev. Saúd. Públic* 37, 714-721, 2003.
[25] Amâncio F.F. Mortalidade e fatores prognósticos em pacientes HIV positivo internados em unidade de terapia intensiva de hospital especializado em doenças infecto-parasitárias. Belo Horizonte (Dissertação de Mestrado em Medicina Tropical - UFMG), 2010.
[26] Silva D.R., Menegotto D.M., Schulz L.F., Gazzana M.B., Dalcin P.T. Mortality among patients with tuberculosis requiring intensive care: a retrospective cohort study. *BMC Infect. Dis.* 10, 54, 2010.
[27] Lindoso A.A.B.P., Waldman E.A., Komatsu N.K., Figueiredo S.M., Taniguchi M., Rodrigues L.C. Perfil de pacientes que evolucionan a óbito por tuberculosis enel municipio de São Paulo. *Rev. Saúd. Públic*. 42, 805-812, 2008.