OBJECTIVE: to describe the clinical and epidemiological characteristics when identifying factors associated with death caused by tuberculosis in the only referral hospital in the Amazon. Method: a descriptive retrospective study, from the review of 162 medical records. The causes of death were obtained from the death certificates. The analysis of factors associated with death was performed by logistic regression using the SPSS 16.0 software. The research project was approved by the Ethics Committee in Research, CAAE n° 0006.0.114.115-09. Results: 17.3% of the patients came to death. Having two or more comorbidities, advanced age, multidrug-resistant tuberculosis, and time of hospitalization <15 days were associated with death. Conclusion: most of the deaths could have been avoided, reinforcing the need of establishment of the role not only of primary care, as well as hospital care, for the adequate control of tuberculosis. Descriptors: Epidemiology; Tuberculosis; Hospitalization; Hospital Mortality; Epidemiologic Factors.

RESUMO
Objetivo: descrever as características clínico-epidemiológicas ao identificar fatores associados ao óbito causado pela tuberculose em pacientes do único hospital de referência do Amazonas. Método: estudo descritivo e retrospectivo, a partir da revisão de 162 prontuários. As causas de morte foram obtidas nas declarações de óbito. A análise dos fatores associados ao óbito foi realizada mediante regressão logística por meio do software SPSS 16.0. O projeto de pesquisa teve a aprovação do Comitê de Ética em Pesquisa, CAAE n° 0006.0.114.115-09. Resultados: evoluíram para óbito 17.3% dos pacientes. Ter duas ou mais comorbidades; idade avançada; tuberculose multidrog-resistente; e tempo de internação <15 dias associaram-se ao óbito. Conclusão: a maior parte das mortes poderia ter sido evitada, reforçando a necessidade do estabelecimento do papel não só da atenção básica, como também da assistência hospitalar, para o adequado controle da tuberculose. Descriptores: Epidemiologia; Tuberculose; Hospitalização; Mortalidade Hospitalar; Fatores Epidemiológicos.

RESUMEN
Objetivo: describir las características clínicas y epidemiológicas cuándo identificar los factores asociados a la mortalidad causada por la tuberculosis en el único hospital de referencia en el Amazonas. Método: estudio descriptivo y retrospectivo, a partir de la revisión de 162 prontuarios. Las causas de muerte se obtuvieron de los certificados de defunción. El análisis de los factores asociados con la muerte se realizó por regresión logística usando el software SPSS 16.0. El proyecto de investigación fue aprobado por el Comité de Ética en Investigación, CAAE No. 0006.0.114.115-09. Resultados: el 17.3% de los pacientes murieron. Tener dos o más comorbilidades, edad avanzada, la tuberculosis multiresistente y la duración de la estancia < 15 días se asociaron con la muerte. Conclusión: la mayoría de las muertes se podrían haber evitado, lo que refuerza la necesidad de establecer no sólo el papel de la atención primaria, pero también la atención hospitalaria, para el adecuado control de la tuberculosis. Descriptores: Epidemiología; Tuberculosis; Hospitalización; Mortalidad Hospitalaria; Factores Epidemiológicos.

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Paleopathological evidences indicate that tuberculosis (TB) is a major cause of illness and death in humans for at least five thousand years. In the 21st Century, TB still stands out for its large magnitude and dispersion, considered the main cause of death associated with an infectious agent. In 2011, for example, approximately 8, 7 million people were affected and 1.4 million died of TB on the planet, confirming their prevalence and social.\(^1\)

In Brazil, tuberculosis manifests are endemic, with detection annual average of about 80.000 new cases in the last five years. However, the distribution of these cases is not homogeneous in the country and the states of Rio de Janeiro, in the southeast, and the Amazon in the north, concentrate the highest rates of incidence and mortality related to the disease.\(^1\)

The TB death should not be common cause of death, on the contrary, should be an extraordinary event and low frequency. Although there are policy guidelines and clearly defined strategies for tuberculosis control in the primary care level,\(^4\) remains high number of patients who are treated and/or diagnosed in hospitals, which not infrequently have severe clinical forms and evolve to death.\(^5\) In general, tuberculosis deaths are associated with serious complications of the disease, unfavorable conditions and diseases, with emphasis on co-infection with HIV/AIDS and diabetes mellitus.\(^7\)\(^-\)\(^10\)

Although the morbidity and mortality from TB Amazonas situated among the worst in the country,\(^3\) studies in this regard are scarce and punctual. When performed, in most cases, are not representative and illustrative of the clinical, epidemiological and social-related TB at the state level.\(^1\)\(^-\)\(^2\)

With regard to studies on disease-related hospitalizations in the Amazon, the gap is even greater, since few studies were found with this approach in the indexed literature, among these, we highlight a study conducted in 2010 in the city of Manaus we identified and analyzed the factors associated with length of stay between HIV positive and negative.\(^13\)

Therefore, this study aims to:

- Describe the clinical and epidemiological characteristics to identify factors associated with death caused by tuberculosis patients in the hospital only reference of Amazonas.

A descriptive and retrospective study hospital based, which included TB patients over 14 years old, admitted to the Hospital Foundation Adriano Jorge (FHAJ) during the year 2009. This health unit was intentionally selected to be the only and main inpatient unit for patients with and without TB co-infection with HIV in the state of Amazonas. During the year 2009, for example, of the 286 hospitalizations for TB in patients over 14 years in the Amazon, approximately 60% were made in FHAJ.\(^14\) The FHAJ is a general hospital of medium and high complexity that also operates as a unit teaching aid and has approximately 250 beds, among which 33 are reserved for specialty Thoracic Association.

The outcome of interest in this study was death with mention of tuberculosis on the death certificate (DO - in Portuguese). For analytical purposes, tuberculosis as a cause of death corresponded to the clinical forms included in the range of categories A15-A19 as well as the category “Sequelae of tuberculosis” (B90), International Statistical Classification of Diseases and Related Health Problems (ICD-10).

These data were collected from the Statistical Service Medical Records (SAME), using a standard form, previously tested.

The reference population was composed of individuals hospitalized and target population for those diagnosed with TB, recorded in the Hospitalization Authorization (AIH) and/or the medical records of FHAJ, during the period January 1 to December 31, 2009. Founded Hospital in Adriano Jorge medical diagnoses are ruled on the standards recommended by the Brazilian Guidelines for Tuberculosis of the Brazilian Thoracic Association.

The records of individuals with a history of hospitalization in subsequent periods (with hospitalizations, where the difference between the high and the date of the last date of the next admission was less than 15 days) were considered as re-hospitalization and were grouped as single event with order not to violate the independence assumption.

After reviewing the medical records, drew up a list of general data identification of patients admitted with tuberculosis in FHAJ during the year 2009. Then, we performed a manual search of death certificates (DO) available at the hospital to check the frequency and the actual contribution of tuberculosis deaths among computed in our study. In this case, we considered the field where there was no mention of the disease,
ie, those who had tuberculosis as underlying or associated cause of death.

We included the following variables: age, sex, city of residence / origin; reason / justification of hospitalization, duration of hospitalization, clinical presentation, type of discharge, and information on multidrug-resistant tuberculosis (MDR-TB). The presence of two or more comorbidities at admission was also considered as an independent variable in this analysis.

Data were analyzed using SPSS - version 16.0 (SPSS Inc., Chicago, Illinois, USA). The chi-square and Fisher exact tests were used to compare proportions. The U Mann-Whitney test was used for comparison of medians. The level of statistical significance was 5%. A multiple logistic regression analysis was preceded by testing and selection of simple regression models, variable between death caused by TB (dependent) and the variables that were associated (independent) to the level of 20%.

The multiple logistic regression models were adjusted following the stepwise forward method, which were introduced in descending order of significance the variables of interest. The final model only those that were significant at the 5% level. The odds ratio (OR) was used as a measure of association. The quality of fit of the multiple regression models were evaluated according to the Hosmer and Lemeshow test.

The research protocol was approved by the Ethics Committee of the institution investigated, CAAE n. 0006.0.114.115-09.

RESULTS

We identified 162 records of patients diagnosed with tuberculosis, 66% (107/162) in men (p = 0.0001). The mean age was 47 years old (15-86 years old, standard deviation: 19.7). The median was 44.6 years old, with no significant difference between genders (p = 0.40).

Altogether, 83.3% (135/162) of the cases were from the capital Manaus, and the others in the state, except for one individual from another unit of the Federation.

The main reason for admission was "impairment of the general", which accounted for 34.6% (56/162) of admissions. Second came the "social causes" 20.4% (33/162) and then the "serious complications of the disease or comorbidities" with 17.9% (29/162) (Table 1).

The mean hospital stay was 31 days (range 1-244 days standard deviation: 38.5) and the median time was 18 days. The variable length of stay was stratified into 3 groups: <15 days (38.9%), 15-25 days (22.8%), and 26 days or more (38.3%) (Table 1).

Pulmonary TB was identified in 84.0% (136/162) of admissions. The multidrug-resistant tuberculosis (MDR-TB), in turn, was recorded at 3.7% (6/162) of patients (Table 1).
In 67.3% (109/162) of cases was recorded the presence of at least one comorbidity. Malnutrition/ cachexia was the most common comorbidity, totaling 16.7% (27/162) of the records, followed by hypertension with 16.6% (26/162) and diabetes mellitus type II with 13.0% (21/162). In about 7% (11/162) of cases was recorded the presence of HIV / AIDS.

Regarding the hospital, the most common type of record was clinical improvement, totaling 76.5% (124/162) of cases, followed by death with 17.3% (28/162) and 2.5% abandonment (4/162). Other causes were recorded in only 3.7% (6/162) of all cases.

The highest percentages of deaths were recorded in patients with pulmonary form, coming from the capital, Male, in which had two or more comorbidities, those with length of stay less than 15 days was 63.2% (12/19) and those older than 65 years with 47.9% (9/19) (Table 1). In all, 19 deaths had TB as underlying or associated cause of death of those, 16 had TB as a cause three as an associated cause of death.

The bivariate analysis revealed that the level of significance of 20%, the variables “MDR-TB”, “length of stay”; “old” and have “two or more comorbidities”; were associated with the occurrence of deaths caused by TB (Table 2).
Factors associated with death caused by tuberculosis in patients at a State hospital, Manaus/AM, Brazil, 2009.

Table 2. Factors associated with mortality caused by tuberculosis in patients at a State hospital, Manaus/AM, Brazil, 2009.

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR Gross (IC 80%)</th>
<th>OR Ajustado (IC 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB-MDR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,0 (1,0-2,0)</td>
<td>1,0 (1,0-2,0)</td>
</tr>
<tr>
<td>Yes</td>
<td>8,7 (2,9-26,3)</td>
<td>27,1 (2,8-257,9)</td>
</tr>
<tr>
<td>Length of stay (in days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 15</td>
<td>2,7 (1,3-5,5)</td>
<td>5,2 (1,4-18,5)</td>
</tr>
<tr>
<td>15-25</td>
<td>0,6 (0,2-2,0)</td>
<td>0,7 (0,1-4,5)</td>
</tr>
<tr>
<td>&gt; 25</td>
<td>1,0</td>
<td>1,0</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 15</td>
<td>1,021 (1,005-1,038)</td>
<td>1,033 (1,004-1,062)</td>
</tr>
<tr>
<td>15-25</td>
<td>1,0</td>
<td>1,0</td>
</tr>
<tr>
<td>&gt; 25</td>
<td>3,1 (1,6-5,9)</td>
<td>3,5 (1,1-11,1)</td>
</tr>
<tr>
<td>2 or + comorbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1,0 (1,0-2,0)</td>
<td>1,0 (1,0-2,0)</td>
</tr>
<tr>
<td>Yes</td>
<td>3,1 (1,6-5,9)</td>
<td>3,5 (1,1-11,1)</td>
</tr>
</tbody>
</table>

In the adjusted model, the variables "two or more comorbidities" and "MDR-TB" increased by 3,5 and 27,1 times the odds of deaths caused by TB, respectively. In turn, the length of stay less than 15 days increased by 5,2 times the odds of deaths caused by TB. The association analysis of the age variable indicates that death with every increase of one year of life increased the risk of death around 3% (Table 2). Another possible interpretation is that each increment of 20 years the chance of death increases by having approximately 93% (exp (20 X 0,033)) (Table 2).

There were no evidence of collinearity between the independent variables and the Hosmer-Lemeshow test showed that the multiple regression model showed a good fit (p = 0,567).

**DISCUSSION**

The percentage of death or mortality (17,3%) observed in individuals hospitalized with TB in FHAJ was quite high and contrasts with the records of most studies on the subject that, in general, indicate percentages below 12%.|15-8|

The low frequency of TB / HIV recorded in our study reinforces the seriousness of the problem, since it is widely accepted in the literature that this disorder is strongly associated with death, relatively common event in inpatient units specialized in caring for patients with AIDS.|6,8|

Paradoxically, our findings showed no association between the presence of AIDS and death in hospitalized patients with TB. This result can be partially explained by the fact that the state reference hospital for AIDS was not included in our analysis.

Although most hospitalizations occurred in individuals living in Manaus, highlighted the percentage of patients from the countryside (15,4%), because data from the Hospital Information System of the Unified Health System (SIH / SUS),|14 related to totality of TB hospitalizations during the year 2009 in the Amazon indicate that almost all (95%) of these hospitalizations occurred in the state capital.

Analogous to that described in the literature, in our study, the most hospitalizations length of stay in hospital was more than 15 days, there was a predominance of men, adults and cases with pulmonary clinical forms.|13 The prominence of pulmonary forms is consistent with the non-inclusion of minors 15 years in our analysis because among children and adolescents extra-pulmonary forms tend to be more frequent than in adults.|19|

The "impairment of general condition", the "social causes" and "serious complications of TB" or "comorbidities" accounted for approximately 73% of admissions, suggesting that admissions occurred in individuals with impaired health status or social risk, as with other national and international studies on the subject.|16,20 These findings call attention to the need for actions and practices of social and health specific should be directed to individuals with these characteristics.

The presence of hypertension, diabetes mellitus and malnutrition ranks among the major comorbidities demonstrate the importance of metabolic diseases in the clinical course of patients with TB, especially among the elderly. In these patients the chance to evolve to substantially increase mortality, particularly when associated with other health problems.|21,2

The observed statistical association between the occurrence of death from TB in the presence of “two or more comorbidities,” reinforces the importance of not only identification, but also the proper management of other diseases, and AIDS, to achieve a favorable outcome in patients with tuberculosis.|11,17,21,23 Data from multiple logistic regression indicated that the odds of death increased with increasing age of patients. A moment in history occurs a progressive aging of the population, recognize older people as a vulnerable group to the TB death.|17,8 seems to be a strategy not only relevant, but necessary, especially during the formulation and implementation of strategies to control disease.
The multidrug-resistant tuberculosis (MDR-TB) has been gaining increasing prominence on the international scene. Second report of the World Health Organization, about 4% of cases occurring in the world is faced with MDR-TB. According to this same document, Brazil received credit for the implementation of successful strategies in the rational use of anti-TB drugs and was not included in the list of 27 priority countries for the control of MDR - TB in the world. However, recent studies indicate that MDR-TB is expanding, with a growing number of cases being reported in various parts of the country, including in areas situated within the Amazon, such as those traditionally inhabited by indigenous populations.

Despite the small proportion of cases of MDR-TB in this study, it was found its association with death caused by TB, reinforcing the negative impact of this condition on the outcome of admissions of patients with the disease. Moreover, the MDR-TB presents significant potential for nosocomial spread, especially in hospitals where basic biosecurity measures are not adequately considered.

The association observed between the occurrence of death caused by TB category and length of stay less than 15 days, indicating that a significant portion of individuals hospitalized with TB patient was in an advanced stage of the disease, at the time of hospital admission, reinforcing the data regarding the main reasons for hospitalization. This information is valuable to health professionals who accept these patients in hospitals, because if the admission is already possible to recognize the risk factors that can potentially worsen the clinical picture, there will be higher chances that patients have a more favorable outcome.

By one side is widely acknowledged that studies guided by data from the Hospital Information System of SUS (SIH/SUS) have limitations due to its essentially administrative, still, this system constitutes an important source of data about the conditions of health, utilization and quality of services. On the other hand, despite the fact that we have not included more variables in our analysis, due to the low quality of these records and the incompleteness of the same, the strategy based on chart review allowed the study of an important set of clinical characteristics epidemiological not catchable from the data available usually by computerized systems.

Even though the odds ratios (OR) obtained from logistic regression have presented confidence intervals wide range - a fact that undermines the accuracy of our estimates - the same cannot be said for the associations observed, because they are consistent with the described in other contexts and may also be useful for understanding the relationships between the clinical-epidemiological factors mentioned and the occurrence of deaths in individuals hospitalized for tuberculosis.

**CONCLUSION**

The observed association between the occurrence of death category and length of stay less than 15 days, indicating that a large part of individuals hospitalized with TB patient was in advanced clinical stage of the disease, at the time of hospital admission, reinforcing the findings relating to the main reasons for hospitalization observed in this study. This serves as a warning to nursing professionals who treat these patients. If the admission is possible to recognize the potential risk factors elucidated here, measures of attention and care will be taken to prevent the worsening of the consequent unfavorable outcome for the patient. Therefore, a well-trained nursing staff, working in an interdisciplinary and integrated can be extremely valuable for proper clinical management and bring benefits to the sensitive treatment, thereby helping to increase survival of patients.

It is recognized that no causal relationship has been demonstrated in this investigation. However, regardless of the limitations of this approach means that our findings may be useful for understanding and explaining the relationship between the occurrence of death in patients hospitalized with tuberculosis and presence of associated factors, such as the presence of two or more comorbidities, advanced age, MDR - TB, and length of stay.

If these factors are taken together, it will be possible for health professionals to predict that cases that meet these characteristics are more likely to progress to death. Therefore, it is evident the need for clear and effective establishment of guidelines and conduct not only in the field of primary care, as well as hospital services, to achieve adequate control of tuberculosis, especially in its severe forms that have a high potential for lethality.

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