**ORIGINAL RESEARCH ARTICLE**

**Factors associated with death among tuberculosis patients followed at Ignace Deen Hospital in Conakry, Guinea**

**Abstract**

**Introduction**: In many countries, large numbers of tuberculosis patients continue to die despite the efforts of control programmes. The aim of this study was to identify the factors associated with death in patients.

**Material and methods:** This was a retrospective cohort study using routine data from the respiratory medicine department of Ignace Deen Hospital in Conakry (Guinea) over a 6-year period (from 1 January 2015 to 31 December 2020). A multivariate analysis using the Cox model was used to identify the factors associated with death, using R software. The significance level was set at 0.05 for the final model.

**Results:** During the study period, 1,579 patients with tuberculosis were seen in the department, of whom 618 were included.The median age was 39, with extremes of 28 and 51. There was a predominance of men (69.90%). The majority marital status was single (71.52%). The main clinical signs were cough (87.38%), chest pain (66.99%) and night sweats (77.35%). Paraclinically, bacilloscopy was positive in 79.77% of cases. The mortality rate was 10%. In multivariate analysis, the factors independently associated with the occurrence of death in patients with tuberculosis were body mass index < 17.5 kg/m2 (adjusted RR = 4.32 [2.28-8.17] ; adjusted p-value < 0.0001); chronic obstructive pulmonary disease (adjusted RR = 10.83 [5.01-23.41]; adjusted p-value < 0.0001); diabetes (adjusted RR = 9.41 [3.63-24.41]; adjusted p-value < 0.0001) and HIV status (RR = 2.67 [1.42-5.03]; adjusted p-value = 0.00229).

**Conclusion:** These results underline the need to strengthen the overall management of tuberculosis patients, particularly those with identified risk factors, by stepping up efforts in the areas of early detection, nutritional support and management of co-morbidities.

**Key word:** Tuberculosis, Factors, Deaths, Hospital, Guinea

**INTRODUCTION**

Tuberculosis (TB) is a communicable disease that is a major cause of morbidity and one of the ten leading causes of death in lower-middle income countries. It is caused by Mycobacterium tuberculosis, which is spread when sick people expel bacteria into the air, for example by coughing. The disease generally affects the lungs (pulmonary TB), but can also affect other parts of the body (extrapulmonary TB) [1]. Although highly effective treatment is available, in 2018 it was estimated that 1.2 million HIV-negative people died from TB and 251,000 people living with HIV died from the disease [2].

Identifying patients at risk of death during TB treatment should be a priority for health surveillance: this is essential for assessing programmatic needs and has the potential to contribute to targeting interventions and improving treatment follow-up [2]. In Ethiopia, the determinants of mortality in TB/HIV patients were reported in two studies. The first showed that being male, bedridden and having a persistent cough were predictive of mortality [3]. For the second, the main determinants were a low body mass index (BMI), a blood albumin level of less than 3 g/dl, an initial CD4 count of less than 50 cells/μL [4]. In Mali, the variables independently associated with patient death were polypnoea, WHO clinical stage IV [5]**.** In Kenya, undernutrition and advanced age were also positively associated with mortality [6]. In Conakry (Guinea), a study revealed that 16.8% of tuberculosis patients were co-infected with HIV. The occurrence of death in this population was significantly associated with the presence of co-morbidities such as hepatitis B, arterial hypertension, diabetes and a CD4 count of less than 200 cells/mm³ [7]**.**

Joint efforts by Guinea's National Tuberculosis Control Programme (PNLT) and its technical and financial partners have helped to reduce the incidence of tuberculosis from 228 cases per 100,000 inhabitants in 2000 to 175 cases per 100,000 inhabitants in 2022. The therapeutic success rate has improved, rising from 80.6% in 2013 to 90.3% in 2022. The mortality rate continues to fall, from 52 to 16 per 100,000 inhabitants between 2000 and 2022 [8].

The aim of this study was to identify the factors associated with death in tuberculosis patients followed up at the Ignace Deen Hospital.

**MATERIEL AND METHODS**

**2.1. Study framework**

The Republic of Guinea is located in West Africa, between latitudes 7 and 12 north and longitudes 8 and 15 west. It is bordered by 300 km of coastline and stretches 800 km from east to west and 500 km from north to south. It has a total surface area of 245,857 km2.

The study took place in the respiratory medicine department of the Hospital National Ignace Deen at Conakry University Hospital. With a hospital capacity of 82 beds, it is the reference department for the treatment of respiratory diseases in the country. It also houses the national reference laboratory for mycobacteria.

**2.2. Type and period of study**

This was a retrospective cohort study using routine data from the respiratory medicine department of Ignace Deen Hospital in Guinea, over the 6-year period from 1 January 2015 to 31 December 2020.

**2.3. Study population and sampling**

**2.3.1. Study population**

The study population consisted of tuberculosis cases registered in the respiratory medicine department of Ignace Deen Hospital in Guinea.

**2.3.2. Sample size**

We used Epi Info 7 to calculate the sample size.

The precision parameter was set at 5%, the proportion at 50% and the margin of error α at 0.05.

The sample size of tuberculosis cases for our study was 618.

**2.3.3. Sampling procedure**

A simple random sample was used. Among the cases of tuberculosis recorded during the study period, 618 cases were selected between 1 and 1579 using the Open Epi software.

**2.4. Study variables**

The dependent variable was the number of deaths. It is of the binary ‘Yes’ or ‘No’ type.

Independent variables: Age, sex, place of residence, occupation, level of education, marital status, clinical signs, co-morbidities, alcohol consumption, tobacco consumption, HIV status, anti-tuberculosis treatment, antiretroviral treatment (ART).

**2.5. Data collection**

The questionnaire developed was pre-tested and any imperfections were taken into account before data collection. Patient medical records, hospitalisation registers, consultation registers and laboratory records were used as sources of information.

**2.6. Data analysis**

The data were analysed using R software version 4.0.1. Quantitative variables were measured by their medians and interquartile ranges. Categorical variables were presented by their frequencies and 95% CIs. A uni- and multivariate analysis using the Cox model was used to identify the factors associated with death. The Kaplan-Meier method was used to estimate the probability of survival as a function of the time from the date of hospitalisation to the occurrence of the last event (death or end of study). The Log-rank test was used to compare survival curves by category. In the multivariate analysis, the top-down Cox stepwise model was used to obtain an adjusted estimate of the association. The interactions of the variables retained in the final model were also checked. The significance level was set at 0.05 for the final model. The results are presented as Relative Risks (RR) with 95% confidence intervals (CI) and corresponding p-values.

**RESULTS**

During the study period, 1,579 patients with tuberculosis were admitted to the department, of whom 618 were included.

The age group most represented was ≤ 35 years (43.37%) with a median age of 39 years and extremes of 28 and 51 years. There was a predominance of men (69.90%). The dominant marital status was single, followed by married with 71.52% and 26.05% of cases respectively.

The majority lived in Conakry (71.68%) and were mainly manual workers (20.87%) (Table I). The main clinical signs were cough (87.38%), chest pain (66.99%) and night sweats (77.35%). Body mass index was < 17.5 kg/m2 in 22.98% of cases. Comorbidities such as diabetes, cancer and constrictive lung disease were found in 9.87% of patients. Pulmonary tuberculosis was found in 94.66% of cases. In terms of paraclinical tests, bacilloscopy was positive in 79.77% of cases. Genexpet was also positive in 77.51% of cases. Chest CT scans were not performed in the majority of cases (98.54%). Co-infection with tuberculosis and HIV was found in 33.66% of cases (Table II). The majority of patients were on anti-tuberculosis treatment (93.04%). Antiretroviral treatment was effective in 16.83% of co-infected patients. Tuberculosis was resistant to treatment in 34.95% of cases.

The median hospital stay was 7 days, with extremes of 4 and 14 days. Sixty-two patients died, representing a mortality rate of 10%. In univariate analysis, the main factors associated with these deaths were BMI < 17.5 kg/m2 (crude RR = 6.24 [3.69-10.53] ; crude p-value <0.0001), chronic obstructive pulmonary disease (COPD) (crude RR = 11.37 [6.88-18.79] ; crude p-value <0.0001), diabetes (crude RR = 5.27 [2.68-10.34]; crude p-value <0.0001), drug-resistant tuberculosis (crude RR = 2.28 [1.38-3.77]; crude p-value = 0.002), HIV status (crude RR = 5.19 [2.93-9.18]; crude p-value <0.0001). In multivariate analysis, the factors independently associated with the occurrence of death in patients with tuberculosis were body mass index < 17.5 kg/m2 (adjusted RR = 4.32 [2.28-8.17] ; adjusted p-value < 0.0001); COPD (adjusted RR = 10.83 [5.01-23.41]; adjusted p-value < 0.0001); Diabetes (adjusted RR = 9.41 [3.63-24.41]; adjusted p-value < 0.0001) and HIV status (RR = 2.67 [1.42-5.03]; adjusted p-value = 0.00229). (Table III).

**Table I :** Sociodemographic characteristics of tuberculosis patients at Ignace Deen Hospital, Guinea, 2015-2020

|  |  |  |
| --- | --- | --- |
| Characteristics | N (%) | 95% CI |
| Age range |  |  |
| ≤ 35 years | 268 (43.37) | [39.51-47.30] |
| > 35 years | 350 (56.63) | [52.70-60.49] |
| Sex |  |  |
| Female | 186 (30.10) | [26.61-33.83] |
| Male | 432 (69.90) | [66.17-73.39] |
| Education | |  |
| No schooling | 416 (67.31) | [63.52-70.90] |
| Schooling | 202 (32.69) | [29.10-36.48] |
| Profession |  |  |
| Civil administrator | 48 (7.77) | [5.91-10.15] |
| Health Officer | 6 (0.97) | [0.45-2.10] |
| Artist | 4 (0.65) | [0.25-1.65] |
| Chauffeur | 91 (14.72) | [12.15-17.74] |
| Driver | 119 (19.26) | [16.34-22.55] |
| Student | 23 (3.72) | [2.49-5.52] |
| Teacher | 18 (2.91) | [1.85-4.56] |
| Housewife | 125 (20.23) | [17.25-23.57] |
| Military | 25 (4.05) | [2.75-5.90] |
| Worker | 129 (20.87) | [17.85-24.25] |
| Not employed | 30 (4.85) | [3.42-6.85] |
| Residence |  |  |
| Conakry | 443 (71.68) | [68.01-75.09] |
| Outside Conakry | 175 (28.32) | [24.91-31.99] |
| Marital status |  |  |
| Single | 442 (71.52) | [67.84-74.94] |
| Divorced (e) | 7 (1.13) | [0.55-2.32] |
| Married (e) | 161 (26.05) | [22.75-29.65] |
| Widow (er) | 8 (1.29) | [0.66-2.53] |
| Consumption of alcohol |  |  |
| No | 162 (26.21) | [22.90-29.82] |
| Yes | 456 (73.79) | [70.18-77.10] |
| Tobacco consumption |  |  |
| No | 567 (91.75) | [89.31-93.67] |
| Yes | 51 (8.25) | [6.33-10.69] |

**Table II :** Clinical characteristics of tuberculosis patients at Ignace Deen Hospital, Guinea, 2015-2020

|  |  |  |
| --- | --- | --- |
| Characteristics | N (%) | 95% CI |
| Comorbidities (diabetes and cancer, COPD) |  |  |
| No | 557 (90.13) | [87.52-92.24] |
| Yes | 61 (9.87) | [7.76-12.48] |
| Toux |  |  |
| No | 78 (12.62) | [10.23-15.47] |
| Yes | 540 (87.38) | [84.53-89.77] |
| Night sweats |  |  |
| No | 478 (77.35) | [73.88-80.47] |
| Yes | 140 (22.65) | [19.53-26.12] |
| BMI |  |  |
| ≥ 17.5 kg/m2 | 476 (77.02) | [73.54-80.17] |
| < 17.5 kg/m2 | 142 (22.98) | [19.83-26.46] |
| Chest pain |  |  |
| No | 204 (33.01) | [29.42-36.81] |
| Yes | 414 (66.99) | [63.19-70.58] |
| Types of tuberculosis |  |  |
| Extra-pulmonary TB | 33 (5.34) | [3.83-7.40] |
| Pulmonary TB | 585 (94.66) | [92.60-96.17] |
| BAAR |  |  |
| Negative | 125 (20.23) | [17.25-23.57] |
| Positive | 493 (79.77) | [76.43-82.75] |
| Genexpert |  |  |
| Négative | 139 (22.49) | [19.38-25.95] |
| Positive | 479 (77.51) | [74.05-80.62] |
| Chest computed tomography |  |  |
| No | 609 (98.54) | [97.26-99.23] |
| Yes | 9 (1.46) | [0.77-2.74] |
| HIV status |  |  |
| No | 410 (66.34) | [62.53-69.96] |
| Yes | 208 (33.66) | [30.04-37.47] |

**Table III :** Multivariate analysis of factors predictive of death in tuberculosis patients at Ignace Deen Hospital, Guinea, 2015-2020

|  |  |  |  |
| --- | --- | --- | --- |
| Probable risk factor | | Adjusted RR 95% CI | p-value adjusted |
| Education | |  |  |
| Schooling | | 1 |  |
|  | No schooling | 0.6710 [0.34-1.32] | 0.24899 |
| Marital status |  |  |  |
|  | Married | 1 |  |
|  | Divorced | 2.0261 [0.39787-10.318] | 0.39519 |
|  | Widowed | 0.3021 [0.06444-1.4168] | 0.12900 |
| Night sweats |  |  |  |
|  | No | 1 |  |
|  | Yes | 1.3456 [0.66042-2.7416] | 0.41368 |
| BMI |  |  |  |
|  | ≥ 17.5 kg/m2 |  |  |
|  | < 17.5 kg/m2 | 4.3204 [2.28274-8.1770] | **< 0.0001** |
| Asthenia |  |  |  |
|  | No | 1 |  |
|  | Yes | 0.9500 [0.33353-2.7058] | 0.92346 |
| TB treatment |  |  |  |
|  | No | 1 |  |
|  | Yes | 0.7208 [0.35690-1.4557] | 0.36127 |
| COPD |  |  |  |
|  | No | 1 |  |
|  | Yes | 10.838 [5.01667-23.414] | **< 0.0001** |
| Diabete |  |  |  |
|  | No | 1 |  |
|  | Yes | 9.4156 [3.63185-24.410] | **< 0.0001** |
| HIV status |  |  |  |
|  | No | 1 |  |
|  | Yes | 2.6735 [1.42097-5.0302] | **0.00229** |

**DISCUSSION**

Death due to tuberculosis is considered a preventable sentinel event. The disease has a simple diagnosis, medicines are available free of charge from the public health network, full treatment with first-line medicines is relatively inexpensive, and the disease is curable in almost 100% of cases. Consequently, the high number of deaths highlights weaknesses in patient management. These deficiencies range from difficulties in accessing diagnosis and treatment in primary care services to access to emergency services and hospitalisation for patients in the advanced stages of the disease [9]. Numerous studies have examined tuberculosis mortality rates in low-income countries and regions with high HIV prevalence [10,11]. However, data on mortality among hospitalised patients with tuberculosis remains limited. Death certificate reports are often inaccurate, and research methodologies have accentuated the reduced reliability of existing data [12]. Research into mortality rates among hospitalised patients with tuberculosis infection is essential in order to accurately identify predictive factors and quantify mortality, which could help to develop effective control measures and reduce these rates [13].

Some studies show that a higher case-fatality rate and a lower survival rate among patients with tuberculosis are observed in the most vulnerable population groups, such as injecting drug users, people living in deprived areas [14], those requiring intensive care [15], people living with HIV [16], individuals with resistance to anti-tuberculosis drugs [17], significant lung destruction [18], and people making inappropriate use of healthcare services [19].

In our series, HIV is a factor associated with the occurrence of death in tuberculosis patients. Patients living with HIV were three times more likely to die. This can be explained by the fact that HIV-infected patients run an increased risk of contracting tuberculosis even when they are taking antiretroviral drugs, and an increased risk of rapidly progressing to active tuberculosis [20,21]**.** On the other hand, tuberculosis increases HIV replication and viral diversification rates, by increasing the production of pro-inflammatory cytokines that increase HIV replication and viral diversity, thereby facilitating immune escape [22]**.** This synergistic effect could be the main cause of the high mortality rate among tuberculosis patients co-infected with HIV [23]**.** In Peru, one of the most striking results concerned the assessment of TB/HIV co-infection, where indigenous people with a history of HIV were 16.5 times more likely to die from tuberculosis than those without a history of HIV [24]. According to the literature, the risk of death due to tuberculosis in a patient living with HIV is 2 to 4 times higher than in a patient with tuberculosis without HIV [25]. This result is also similar to that of a study carried out in Paraguay, where mortality linked to all forms of tuberculosis was studied for the first time in the country [26].

Data show that diabetes triples the risk of developing tuberculosis [27] and is also associated with poor TB treatment outcomes [28].

Patients with both TB and diabetes have more severe symptoms, higher mortality and an increased risk of relapse compared to TB patients without diabetes [27, 29]. Individuals with poor glycaemic control are more likely to develop active tuberculosis [30] and have poorer therapeutic outcomes [31]. In our study, the association between diabetes and death in tuberculosis patients was statistically highly significant. A study by Camara A et al [7] also showed a statistically significant association.

We found that patients with a body mass index (BMI) < 17.5 kg/m² had more than 4 times the risk of death than those with a higher BMI. This result is higher than that of Camara A. et al. [7], who reported a doubled risk. Several other studies have also confirmed a significant association between low BMI and the occurrence of death in TB patients, underlining the crucial role of malnutrition as an aggravating factor. Patients with COPD were 11 times more likely to die than those without COPD. Our result is superior to that of Da Silva Escada et al [32], who found a 3-fold increase in the risk of death. This is reflected in the delay in diagnosis and the lack of appropriate treatment.

Since TB-related death occurred early in the treatment course, patients with TB with risk factors require intensive monitoring, such as hospitalization or short-term outpatient follow-up, particularly in the early stages of treatment [33]. Nowadays, special attention must also be given to antituberculosis drug resistance. While the prevalence of acquired drug resistance decreased due to due to implementation of DOTS-Plus program, the prevalence of primary drug resistance due to transmission remained high. Greater efforts should be made to screen drug resistance for case finding and to reduce transmission through improving the treatment and management of drug-resistant patients [34].

One of the main limitations of this study is the incompleteness of some of the data, particularly hospital records, consultation registers and collection tools. This lack of literature may have limited the analysis of certain factors potentially associated with mortality, such as socio-economic status, compliance with treatment and access to care. This lack of data may lead to selection or information bias, limiting our ability to explore exhaustively all the determinants of mortality in tuberculosis patients. It could also affect the accuracy of statistical estimates, hence the need to strengthen systems for collecting and archiving clinical data in healthcare facilities, in particular by digitising medical records and providing ongoing training for healthcare workers on the importance of data quality.

**CONCLUSION**

Mortality among tuberculosis patients treated at Ignace Deen Hospital in Guinea remains high. This mortality is significantly associated with several clinical and biological factors, including the presence of co-morbidities, HIV infection, a BMI <17.5 kg/m², and certain chronic respiratory conditions.

These results underline the need to improve the overall management of tuberculosis patients, particularly those with identified risk factors. The Ministry of Health and Public Hygiene must step up its efforts in terms of early detection, nutritional support and management of co-morbidities. It is also essential that healthcare providers are trained to identify and rigorously monitor high-risk cases. Finally, improving the completion of data collection tools and introducing systematic follow-up will contribute to better assessment and more effective management, thereby reducing complications and mortality linked to tuberculosis.

**CONSENT**

Verbal informed consent was obtained from each parturient who was not screened.

**ETHICAL APPROVAL**

The study protocol was approved by the approval committee of the Faculty of Health Sciences and Techniques at the Gamal Abdel Nasser University in Conakry.

Participants' anonymity and confidentiality were respected.

**LIABILITY WAIVER (ARTIFICIAL INTELLIGENCE)**

Generative AI technologies such as large language models (ChatGPT, COPILOT, etc.) and text-image generators were not used in the writing of this manuscript.

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