Risk of dying among tuberculosis patients

MAN MILENA ADINA*, ANTIGONA TROFOR**, DANA ALEXANDRESCU***, ELENA 
DANTES****, POP MONICA*, RUXANDRA RAJNOVEANU*, COSMINA BONDOR*
UMF Iuliu Hatieganu Cluj*, UMF Iasi**, UMF Brasov***, UMF Constanta****
Cluj Napoca, Hasdeu 6 Street
ROMANIA
manmilenaadina@yahoo.com

Abstract: - Tuberculosis (TB) is one of the first worldwide 10 causes of disease. Diminishing mortality risk by TB is an important indicator of successful TB control in society. We conducted a survey from January 1998 to December 2004 on 100 patients who died in Cluj Napoca Pneumology Clinical Hospital by comparison with a second group of 120 TB patients with a favourable evolution. We introduced in the study patients confirmed with TB diagnosis, without coexistence of HIV+ status or any malignancy. We analyzed influence of age, gender, area of residence, smoking status, alcohol abuse, family and environment TB history on Tb resolution outcomes. Special consideration was given to radiological findings, main causes of death, treatment regimens and compliance. Statistical data with analysis of the two groups included in the study aimed to reveal most important mortality risk factors in TB patients and assessment of the relative risk. We found higher mortality in TB patients with concurrent disorders and lack of compliance with an OR of 11.84 as another important risk to increase TB mortality. We concluded identification of risk factors for mortality among TB patients can improve the management of TB cases and avoid increased mortality in such patients.

Key-Words: - tuberculosis, mortality risk, TB mortality, relative risk, TB control

1 Introduction

Tuberculosis is known as one of the first 10 causes of death worldwide (1) In 2000, 8 million people were estimated as TB infected and other 2 million died due to Tuberculosis, thus mortality still remains high among pulmonary TB patients. (2) The World Health Organization (WHO) defines TB mortality as the number of TB cases dying during treatment, regardless of cause. TB mortality is an important indicator of the success of TB control. TB mortality can usually be reduced more quickly than disease incidence, as treatment is beneficial to both disease transmission and case fatality. (1)

2. Problem Formulation

We tried to identify what risk factors are associated with high mortality among tuberculosis patients under treatment. Also, we evaluated the main causes of death.

2.1. Materials

We conducted a retrospective study on two batches. One group - 100 patients diagnosed with pulmonary TB who died in the Hospital “Leon Daniello” of Cluj between 1998-2004. The second group was made of 120 pulmonary TB random patients registered with a favourable treatment evolution in the Hospital “Leon Daniello in Cluj. Inclusion criteria were: patients diagnosed with TB based on bacteriological confirmation. Exclusion Criteria: extra pulmonary TB, HIV+ patients, any concomitant malignancy

2.2. Methods
Clinical data were obtained from medical records. We compared demographic characteristic, disease clinical picture, radiological findings, sputum smears and culture, treatment regimens/evolution, main causes of death. The data were compared between the group of patients who died and the group who survived during hospitalisation. Statistical analyses were performed using SPSS 13.0. Software version variable with a PL 0.05 was considered as having statistically significant. OR =Odds ratio – risk of dying. Hazard ratio over 1 represented a risk factor. 95% confidence interval was used to report the result.

3. Problem Solution

Studying the determinants of death in TB patients could help both the public health professionals and the clinicians to identify vulnerable individuals and important factors to raise necessity of stronger TB control measures. The mortality evolution in our hospital between 1998-2004 is shown in graphic1. We can observe a decrease of TB mortality. Only in 2006 we observed increasing TB mortality to 5.7%.

Demographic characteristics .In group 1 (deceased patients) we found 84% men (16% female). In group 2 ( favourable TB outcome) we have found 17.5% women. Men: women OR=1.11 CI 95% 0.52-2.41 p=0.77. Gender is not prognostic factor for Tb attributable deaths.

The mean age of the patients included in group 1 was 55, 55 yrs; mean age of group 2 was 44, 83 yrs.. Age was a significant prognosis factor (p=0.001). Patients over 50 years had a high risk of death, a higher frequency of a typical clinical features, more adverse TB drugs reactions and greater TB related mortality than younger people.

Mortality evolution

![Graphic 1. Mortality evolution](image)

graphic 2. Age repartition

The patients’ area of residence was predominantly urban (81% in group 1), like the patients of second group (52 %) and urban residence was a significant prognostic factor p=0.002 (OR=2.65 CI 95% 1.37-5.17 )

Occupation was a significant prognosis factor. Retired subjects had a relative risk of death. (Retired: p=0, 01 OR = 1.99 CI 95% 1.09-3.64), other employed categories were not statistically significant. People with superior level of education have poor risk of TB and of death due to underlying TB disease.

![Graphic 2. Age repartition](image)
Graphic 3 Occupation repartition

TB history family was a significant prognostic element probably through poor socio-economical condition, (OR=4.55 CI 95% 1.74-12.39  p=0.0004) .In group 1 we had 22 patients with TB history in their family and only 7 patients in Group .

Homeless and insalubrious home were statistically significant prognostic factor. (P=0.00000002) OR=5.90 CI 95% 3.08-11.39. In group 1, 40 patients had insalubrious home and 17 were homeless; in group 2 only 6 subjects were homeless and 16 had poor socio-economical staus.

Alcohol abuse (84% in group 1 and 71,66% in group 2).Smoking status: active and former smoking was associated with increased mortality among TB patients.

Graphic 4 alcohol and tobacco abuse

Smoking causes damage to the lungs and at systemic level, which could contribute to increased number of deaths by TB. OR=2.33 CI 95% 1.14-4.75 But all the patients smoked and this is not a death risk factor.

Co-morbidity (graphic5) is associated with death in some studies. Factors such as chronic obstructive pulmonary disease, alcohol abuse, diabetes, tobacco smoking was not relevant. The higher risk in the elderly is partly due to increased co morbidity burden (3). In our study, only alcohol abuse is a death risk factor. The other diseases were not revealed as death risk factors.

Graphic 5 Co-morbidities

Co-morbidities

The main symptoms fever, cough, dyspnoea, haemoptysis, increased body weigh, appetite loss, thoracic pain are not associated with death
Impaired general condition is a risk factor for death, and significant statistic OR=4.52 CI 95% 2.24-9.30 p=0.000002

The radiological findings –cavitations, nodular infiltration, consolidation, interstitial, miliary, extended lung lesions are associated with an increase in mortality.

All patients have bacteriologic confirmation and positive bacteriology is associated with increased mortality among patients with TB. Positive smear (M+), and positive culture (C+) were risk factors for death OR=4.57 CI 95% 2.32-9.06 p=0.000001

Bacteriological Confirmation for death patients

After diagnosis, anti TB drugs were prescribed immediately. Treatment failures as relapse and chronic TB were associated with increase of mortality. OR=56.03 CI 95% 21.48 – 152.87 p=0.00000000001

Previous history of TB was associated with death. OR=56.03 CI 95% 21.48 – 152.87 p=0.000000000001 In the present study, a previous history of TB was defined as a past episode of curative combination therapy with anti-TB drugs for ≥1 month Treatment for TB was in standard formula, with regimen I, II or individualized type (when we have resistance or side effects). In group 1, we had 7 patients with regimen I, 62 with regimen II and 31 with individualized treatment. For group 2, we had 94 patients with regimen I, 22 with regimen II and only 4 with individualized treatment.
Causes of death were described in graphic 9. TB related death was defined as one where the underlying or associated cause of death indicated on the patient’s death certificate was anyone of categories A15-A15 of the 10th International Classification of Diseases.

Graphic 9 Causes of death

An important percentage of the patients who died with active tuberculosis died because coexisting medical problems.

Non adherence to prescribed treatment regimens was the most important risk of death factor. OR=11.84 CI 95% 5.68-25.07 p=0.000000000001. Adherence to treatment can protect and increase the survival (OR=0.05 CI 95% 0.02-0.10 p=0.000000000001)

4. Discussion and conclusion

Although tuberculosis mortality has reached very small percentage in the developed world, the proportion of pulmonary TB cases who die in most countries of the European Union is one of the highest in the world (higher than other infection disease) 8% overall (3). At bivariate analysis (made by Lefebvre and col) death was significantly associated with the following factors: male sex, age > 19 years, pulmonary TB, previous history of TB (3). Vasankari and col. noted poor outcomes associated with imunosupression and advanced age, with frequent co-morbidity, stress, a low threshold of suspicion, availability of rapid diagnosis. (4) The association with male sex could be a consequence of repeated short treatment interruptions among males, as has been documented in different settings; better case-holding may improve outcomes (3) MDR was associated with death nearly twice as great in cases with previous history of TB, greater for secondary MDR than for primary MDR. (3). Low and other previous studies have shown than older age, comorbidity, or chest X-ray are associated with increased mortality among patients with TB (6). In his study, Low affirms that cavity does not increase TB mortality (6). Delays in the diagnosis and treatment of pulmonary TB with MDR and HIV infection have been recognised as main causes of death. (2). Irregular treatment was associated with an increased mortality rate among patients with TB. Treatment discontinuation had a profound impact on mortality among patients with TB during war. (5) Early diagnosis, early drug susceptibility testing and the use of adequate medication are crucial to avoid the emergence and propagation of drug resistance. (3,7,8) In many tuberculosis patients, multiple causes of death may act simultaneously, so the cause of death may not be determined with accuracy. Borgdorff and col concluded that cause of death were due to TB misclassification(9). Davis observed the association between prompt recognition and treatment of associated medical problems and re-evaluation of treatment of difficult TB cases could decrease mortality (10) The risk of mortality, once patients with TB are hospitalized, is high and it is unlikely to be explained this situation by the HIV epidemics. Older patients with co-morbidities and patients admitted to the hospital through the emergency department have the highest risk of death. This underscores the importance of the need for improved clinical management strategies that are targeted for high-risk populations, including older patients and those with co-morbidity (11). Strict adherence to correctly prescribed treatment regimens and increased patients’compliance can diminish mortality among TB patients. The WHO (World Health Organisation) used the number of TB deaths divided by the proportion of incident cases who died as one of four approaches to estimate TB incidence (7). The identification of prognostic factors is valuable due to the following three reasons: 1. Optimum treatment may be selected for each patient 2.
Various therapeutic strategies could be compared among groups of patients with similar recurrence risks and treatments. The knowledge that allows the identification of recurrence patterns may be improved and new treatment strategies established. Tuberculosis is still a serious disease even in developed countries. Mortality occurs mainly in risk groups that can be identified at the start of treatment. Identifying mortality risk factors among TB patients can improve the management of TB cases and should avoid increased TB mortality.

References:

Bibliography
5. Per Gustafson, Victor Gomes, Cesaltina Vieira, Henrik Jensen, Remonie Seng, renee Norberg, „ Tuberculosis Mortality during a civil war in Guinea-Bissau „ JAMA 2001, 286; 599-603
11. Nadia N. Hansel, Barry Merriman, edward haparik, Gregory Diette „ Hospitalization for tuberculosis in United States in 2000- Predictor of In-Hospital mortality” Chest 2004,126,1079-1089