

Predictive Factors Of Sequelae Of Pulmonary Tuberculosis: Results Of A Moroccan Cohort

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Abstract:

Introduction: Tuberculosis is a highly contagious and common disease in Morocco, the severity of which is related to several factors, including the occurrence of sequelae. The aim of this study was to define the factors that promote the development of sequelae in pulmonary tuberculosis patients.

Methods: Retrospective cohort of 390 tuberculosis patients whose diagnosis and follow-up of the disease were ensured at the pneumo-phthisiology department of the Mohamed V military hospital in Rabat during the years 2021 and 2022. We calculated the relative risk of the occurrence of sequelae of pulmonary tuberculosis in patients exposed to the following risk factors: Sex, smoking, history of chronic diseases, history of tuberculosis, duration of evolution of symptoms before the first consultation, extent and type of pulmonary lesions at the time of diagnosis.

Results: 130 patients with the criteria were included. The incidence of sequelae of pulmonary tuberculosis in our study was 49.2%. The relative risks (RR) of sequelae in tuberculosis patients were as follows: men (1.22), smokers (1.55), those with chronic diseases (1.43), those with a history of tuberculosis (1.47), patients with chronic disease (1.59), and those with extensive lesions (4.35).

Conclusion: Smoking, the time elapsed before the first consultation, and the extent of lesions are the validated risk factors for sequelae in tuberculosis patients in our study

Keywords: tuberculosis; sequelae; risk factors; lung.

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I. Introduction:

Tuberculosis is a highly contagious infectious disease caused by Koch's bacillus (BK) or *Mycobacterium tuberculosis* [1]. A major public health problem due to its frequency, high cost, and potentially severe progression, the cost of managing tuberculosis in 121 low- to middle-income countries reached US\$6.5 billion in 2020. Tuberculosis is considered among the top ten causes of death worldwide, with approximately 1.4 million deaths recorded. Globally, approximately 10 million people contracted tuberculosis in 2019. In Morocco, approximately 30,000 cases of tuberculosis are recorded each year, with an incidence rate of 87 cases per 100,000 inhabitants, half of which are pulmonary [1]. The severity of the disease is also attributed to the sequelae which can complicate the prognosis, indeed the sequelae of tuberculosis are present in 60 to 90% of patients [2,3], this post-acute phase is currently defined by post-tuberculous pulmonary disease [2], the burden of disability-adjusted life-years (DALYs) linked to tuberculosis and its consequences is considerable since the total of DALYs linked to tuberculosis in 2019 reached 122 million of which 58 million were attributed to post-tuberculous pulmonary disease [4]. Data in the Moroccan literature concerning these sequelae are very limited. The aim of our study is to determine the risk factors for the occurrence of sequelae in patients treated for pulmonary tuberculosis in Morocco.

II. Methods:

- Study design:

This is a retrospective cohort study conducted on 390 tuberculosis patients whose diagnosis, treatment, and follow-up were provided within the pulmonology department at the Mohammed V Military Teaching Hospital in Rabat during 2021 and 2022.

The Mohammed V Military Teaching Hospital in Rabat is a hospital facility of the Royal Moroccan Armed Forces that serves military patients and their families residing in the Rabat-Salé-Kenitra, Tangier-Tetouan-Al Hoceima, and Casablanca-Settat regions.

-Patients:

390 tuberculosis patients were recruited, both men and women, aged 16 years and older. The patients included in this study had isolated pulmonary tuberculosis or pulmonary tuberculosis associated with other sites of infection, and their diagnosis was made according to the recommendations of the World Health Organization (WHO) and the National Tuberculosis Control Program in Morocco. These are cases of pulmonary tuberculosis confirmed by one of the bacteriological methods: direct examination, culture, or the Xpert MTB/RIF test on sputum smears collected in the morning on an empty stomach at the bacteriology laboratory from patients with clinical and/or radiological signs suggestive of the disease. They also include cases of pulmonary tuberculosis diagnosed clinically based on a combination of radio-clinical, biological, and/or histological findings in the absence of bacteriological confirmation [5].

Treatment and its clinical, bacteriological, and radiological follow-up are carried out according to the PNLAT guidelines, with bacteriological examination of sputum smears every two months until the end of treatment and radiological follow-up at the end of treatment and at 3 and 6 months afterward to look for any pulmonary sequelae [5].

The sequelae of pulmonary tuberculosis are defined by the persistence of lesions on radiographs for at least 6 months with negative TB tests and an obvious clinical improvement [6].

Patients with tuberculosis presenting with isolated extrapulmonary involvement, patients transferred to another healthcare facility, and those who discontinued treatment for any reason were excluded. Patients whose treatment was incomplete and whose medical records were uninterpretable were also excluded from this study.

The significance of the risk factors studied was analyzed according to two groups (G1 and G2): Group 1 (G1) consisted of patients with pulmonary tuberculosis who had completed their anti-tuberculosis treatment but still had pulmonary sequelae, while Group 2 (G2) consisted of patients with pulmonary tuberculosis who had completed their treatment but had no pulmonary sequelae.

-Data collection:

Data was collected from the medical records of tuberculosis patients by pulmonologists and resident physicians assigned to the pulmonology department.

-Data management:

Data entry and validation were performed using Excel.

Age, weight, and body mass index were expressed as mean $\pm$ standard deviation (SD).

Sex and smoking status were expressed as a percentage (%) of the sample size.

The explanatory variables or risk factors explored were expressed as absolute numbers (number of cases that developed sequelae of tuberculosis in patients exposed and in those not exposed to a risk factor studied):

Sex, smoking, history of chronic diseases, history of tuberculosis, duration of symptoms before the first consultation (less than 3 months or more than 3 months), single or multiple lung lesions, and the presence of a cavity as a radiological lesion at the time of diagnosis.

The relative risk (RR) of developing sequelae was calculated for each risk factor explored.

To test whether the association between a risk factor and the disease was significant, the Mantel-Haenszel chi-square test was used, with the 95% confidence interval (95% CI) of the RR calculated using Miettinen's method.

III. Results:

A total of 130 patients meeting the criteria were included, and the incidence of sequelae of pulmonary tuberculosis was determined for each risk factor explored.

In our study population, the mean age was 35.2 ± 13.5 years, the mean weight was 64 ± 21 kg, and the mean body mass index (BMI) was 21 ± 2.5 kg/m². Males were the predominant sex, representing 86.9% (113 patients). Smokers represented 37.6% (49 patients) of the study population.

The incidence of sequelae of pulmonary tuberculosis in our study was 49.2%.

Depending on each risk factor, the proportion of patients who developed sequelae and that of tuberculosis patients without sequelae were detailed in Table 1.

	With sequelae (n)	without sequelae (n)
Sexe :		
Men	57	56
Women	7	10
Smoking :		
Smoker	31	18
No smoker	33	48

chronic diseases :		
Yes	12	6
No	52	60
case definition:		
Recurrence	7	3
New cases	57	63
Duration of evolution before consultation:		
Superior by 3 months:	36	22
Inferior by 3 months	28	44
Distribution of radiological lesions:		
Extended	51	16
Limited	11	52

Table 1: Occurrence of sequelae in pulmonary tuberculosis patients according to the risk factors studied.

The relative risk (RR) of sequelae in tuberculosis patients according to sex was 1.22 with a chi-square (χ^2) of 0.91, which is lower than the value of 3.84 found in the chi-square table, corresponding to $p = 0.05$.

The RR of the occurrence of sequelae in pulmonary tuberculosis patients who smoked compared to non-smokers was 1.55, with a χ^2 of 6.19, which is higher than the χ^2 value, corresponding to $p = 0.05$, with a 95% confidence interval [1.09–2.18].

The relative risk (RR) of sequelae in patients with a history of chronic diseases was 1.43 ($\chi^2 = 2.54$).

The RR of sequelae in patients previously treated for tuberculosis compared to new cases was 1.47 ($\chi^2 = 1.86$), which is less than the value corresponding to $p = 0.05$.

The RR in patients with a disease course of 3 months or more compared to those with a disease course of less than 3 months was 1.59 ($\chi^2 = 6.90$, 95% CI [1.12–2.24]).

When lung lesions were extensive, the RR of the occurrence of tuberculosis sequelae was 4.35 ($\chi^2 = 44.78$, 95% CI [2.82–6.69]).

IV. Discussion:

Among the risk factors studied, only smoking, the time elapsed before the first consultation, and the extent of lesions were validated risk factors for the development of sequelae in pulmonary tuberculosis patients in our study. Male sex, a history of chronic diseases, and a previous episode of tuberculosis were not considered risk factors because the association was not statistically significant. The extent of pulmonary lesions at the time of diagnosis was the main factor, with a relative risk (RR) of 4.35 (95% CI [2.82–6.69]).

Nicolas Menzies and colleagues emphasize the persistent inequalities in the follow-up of active tuberculosis. Indeed, the sequelae of tuberculosis are associated with significant morbidity, with a reduction of more than 16 years of life in countries with a high burden of tuberculosis according to the WHO, the sequelae most often occur in the lungs following the irreversible destruction of the lung parenchyma by *Mycobacterium tuberculosis* (Koch's bacillus). They are primarily associated with chronic obstructive pulmonary disease, bronchiectasis, pulmonary hypertension, and frequent superinfections [7].

Of the approximately 155 million survivors treated for tuberculosis since 1980, up to 27% (potentially as high as 80%) may suffer from sequelae of tuberculosis [7,8]. In our study, sequelae were recorded in 49.2% of patients. In a retrospective study of 91 tuberculosis patients with sequelae, males were more affected (64.8% of cases), and extensive bilateral lesions were observed in 40.6% of patients [9], in another series of 30 tuberculosis patients with sequelae, 29 patients with a history of pulmonary tuberculosis, smoking was found in 60% of these patients [10]. Studies focusing on risk factors for the development of sequelae from tuberculosis are considerably limited, and even more so in Morocco. However, there are studies exploring the determinants of mortality related to pulmonary tuberculosis. In Morocco, a retrospective study of 1803 tuberculosis cases, including 46 deaths, shows that male sex (male-to-female ratio = 2.28), smoking (in 50% of deaths), a history of chronic diseases (43% of cases), and extensive bilateral lesions (76% of cases) are considered among the risk factors for tuberculosis mortality [11]. Regarding the time to diagnosis, in most studies, the median time to diagnosis is between 60 and 90 days [12]. This is the time frame considered in our study, where we showed that patients with a diagnosis exceeding 90 days before their first consultation had a relative risk (RR) of 1.59 (95% CI [1.12–2.24]). According to a cross-sectional survey of 219 tuberculosis patients in Kilimanjaro, Tanzania, the incidence of sequelae was 91% of participants, and the identified risk factors were advanced age, smoking, and unfavorable socioeconomic conditions [13]. In our study, the impact of advanced age on the occurrence of sequelae was not investigated since most of the tuberculosis patients included were young, with a mean age of 35 ± 13.5 years. Socioeconomic conditions were also not explored. Our study is a cohort study conducted at the Rabat Military Hospital, which serves military personnel and their families residing in the central and northern regions of Morocco. Data collection was done prospectively, and this data is collected by doctors accurately during regular follow-up of patients without any loss to follow-up during this follow-up, thus reducing information bias. We can strengthen the statistical importance of our results, especially for the two factors:

smoking and disease progression before the first consultation, by extending the duration of the study in order to recruit more cases and thus reduce the selection bias encountered in this work. Despite these limitations, the results obtained remain valid and are consistent with the results in the literature.

By highlighting the risk factors for post-tuberculosis lung disease, we can emphasize the importance of early tuberculosis screening, particularly in high-risk individuals; the importance of smoking cessation, especially in countries with a high incidence of tuberculosis such as Morocco; and the usefulness of regular and structured follow-up of patients completing their anti-tuberculosis treatment. The aim of this follow-up is the early diagnosis of sequelae and the appropriate management of resulting complications, thereby preserving respiratory function and overall survival. The number of tuberculosis survivors in 2020 was 10 times greater than the annual incidence of tuberculosis, hence the importance of focusing the efforts of tuberculosis control programs worldwide on this patient group [8].

V. Conclusion:

The sequelae of pulmonary tuberculosis are frequent and have significant health and socioeconomic repercussions. Understanding their contributing factors facilitates their management.

Conflicts Of Interest:

The authors declare no conflicts of interest.

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