

and isoniazid (HR), and three months of rifapentine and isoniazid.⁵

The Center of Pneumological Diagnosis of Coimbra has implemented, since 2009, a protocol for screening tuberculosis in social solidarity institutions in order to eradicate tuberculosis and prevent new cases in this risk population. The objective of our study was to analyze the results of Tuberculosis screening in residents and employees of several social solidarity institutions in Coimbra, namely "Farol Institution", "Caritas", "Integrar", "Sol Nascente", "Casa Abrigo", "Ateneu" and "Cozinha Económica", over 10 years.

Our study was a retrospective analysis of the clinical processes of residents and employees of these institutions, submitted to screening from the beginning of the project (10 years). Demographic and clinical data were analyzed. Statistical analysis was done using Microsoft Excel.

We included 601 individuals (559 residents and 42 employees), 58.2% male, aged 19–67 years. In our sample the risk factors for tuberculosis were HIV infection (n=39; 7%), alcoholism and drug use (n=246; 44%) and homelessness (n=274; 49%). LTBI screening was done excluding active disease (medical evaluation with a clinical history and chest radiography) and the assessment of immune response to *Mycobacterium tuberculosis*. To diagnosis LTBI we used both tuberculin skin test and the IGRA test.

There were 115 cases (19.1%) of LTBI and 6 of active disease (1%). Ten individuals (1.7%) did not attend screening. All cases of LTBI and active disease were found in residents of those institutions. No cases of LTBI and active disease were observed in the employees.

The majority of the individuals with LTBI (n=99; 86%) completed the treatment. Three individuals are still ongoing therapy, 6 were lost to follow-up and 7 developed pharmacological toxicity, namely hepatotoxicity to isoniazid.

Regarding treatment for LTBI, 68.7% (n=79) started the regimen with HR, and 94.9% (n=75) completed the therapy. Thirty six (31.3%) initiated only H, and 66.6% (n=24) completed the therapy. Regarding treatment for active disease, five individuals completed the treatment with HRZE (isoniazid, rifampicin, pyrazinamide and ethambutol) and 1 HIV + person with rifabutin instead of rifampicin.

In conclusion, our study shows that the majority of the diagnoses of screening of tuberculosis in this risk population were classified as LTBI. Therapeutic adherence was better with the HR regimen. The diagnosis and treatment of LTBI should be properly controlled, and the screening of social solidarity institutions with risk populations could be a move forward in the approach to tuberculosis, as it could help

to avoid new cases in the future and, consequently, reduce the transmission of the disease. The choice of treatment regimen should take into account the efficacy, compliance and associated side effects.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Insights into tuberculosis: A survival analysis of time to recurrence in Portugal, between 2002 and 2009



Recurrence of TB has been associated with poor adherence to treatment, smoking, alcoholism, unemployment, drug abuse, the severity of pulmonary cavitation, HIV infection and duration of treatment.¹ However, the risk factors

can vary considerably across countries and between studies. Since little is known about risk factors for recurrence in Portugal, we aimed to identify predictors of treatment recurrence in the country. Surveillance data on TB for the period of 2002–2009 was provided by SVIG-TB, a database from the Portuguese National Health System. For this analysis, only cases of confirmed TB disease were considered, and patients that had information on the first and second TB episodes. The variables studied were chosen as TB risk

Table 1 Hazard ratios and 95% confidence intervals for TB recurrence.

| Variables | β (se) | HR | CI (95%) | p-value |
|---------------------|---------------|-------|---------------|---------|
| Treatment outcome | 2.32 (0.197) | 10.18 | [6.90, 14.93] | <0.001 |
| Prison | 1.31 (0.522) | 3.63 | [1.41, 10.81] | 0.012 |
| HIV | 0.85 (0.202) | 2.34 | [1.58, 3.48] | <0.001 |
| Clinical form | 0.77 (0.235) | 2.14 | [1.35, 3.40] | 0.001 |
| Alcohol use | 0.62 (0.195) | 1.86 | [1.26, 2.74] | 0.002 |
| Age | -0.01 (0.006) | 0.99 | [0.98, 0.99] | 0.033 |
| Length of treatment | -0.12 (0.021) | 0.90 | [0.86, 0.93] | <0.001 |
| Diabetes | -1.61 (1.007) | 0.20 | [0.03, 1.44] | 0.110 |

se, standard error; HR, hazard ratio; CI, confidence interval.

factors according to previous reports about TB recurrence. The existence of missing data was assessed and missing data characterised (missingness between 0 and 10%). From this characterisation, we chose to explore multiple imputation using random-forest based on multivariate imputation by chained equations. We used a semi-parametric Cox regression model in which the event of interest was the second episode of TB, with time being measured from the end of treatment for a first TB episode. Patients without the second episode of TB before the end of the study were eliminated. A total of 8364 individuals were analysed, of which 145 (1.73%) had a recurrent TB episode during the time of the study.

Patients who defaulted TB treatment are ten times more likely to suffer a recurrent case of TB (Table 1). As expected,¹ HIV was positively associated with recurrence of TB disease (Table 1). Alcohol use disorders have been associated with recurrent TB, mostly by linkage to other confounding factors.^{1,2} We found that even when considering treatment default, TB patients with an alcohol use disorder still had 86% increase in the risk of TB recurrence (Table 1). Incarceration is a known risk factor for TB mainly due to overcrowding, delayed diagnosis and/or inadequate treatment. Our study shows that in Portugal, the risk of TB recurrence for prison inmates is four times higher (Table 1). The standard 6-month treatment regimen is often insufficient to prevent TB relapse,³ nevertheless, the study of treatment length as a risk factor has been mostly restricted to TB patients living with HIV.⁴ Longer treatments are usually prescribed for patients with poor prognosis, potentially confounding a beneficial effect. We found a decrease of 10% in the risk of recurrence per added month of treatment, even accounting for the effect of other risk factors (e.g. HIV), which may suggest a need to reevaluate standard treatment regimens (Table 1). The inclusion of the clinical form in a study about recurrence is unusual. Most studies discard extrapulmonary TB cases since this form is much less infectious, contributing less to overall TB epidemics.¹ Nevertheless, we found that there is a two-fold increase in the risk of recurrence when suffering from an extrapulmonary form of the disease (Table 1). Driver et al.,⁴ showed that in TB patients living with HIV, extrapulmonary disease increased the risk of recurrence, and Millet et al.,² suggested that this was true irrespective of HIV status. Interestingly, some TB risk factors have been shown to be associated with the clinical form – i.e. having HIV or being young increases the chance of having an extrapulmonary infection, while smoking and living with diabetes increases

the chance of a pulmonary TB. Regardless of the association between youth and extrapulmonary TB, the role of age in TB recurrence is somewhat uncertain, with some studies⁵ indicating a decrease of risk for older people while others⁶ suggest a reduction for younger individuals. In Portugal, we found that an increase of one year in the age of the patient leads to a decrease of 1% in the risk of a recurrent episode (Table 1). The association between diabetes and TB incidence has been relatively established, but the association with TB recurrence is unclear.³ Although the variable is not significant, we have estimated a decrease of 80% in the risk of a recurrent episode when having diabetes (Table 1). In this study, 55% of recurrence occurred in the first 12 months after treatment completion, suggesting that in Portugal most of TB recurrence cases were due to relapse since relapse occurs not long after the end of treatment.⁷ Nevertheless, future studies should consider the inclusion of mycobacterial DNA information to distinguish between relapse and exogenous reinfection.

To the best of our knowledge, this is the only study, to date, covering risk factors for TB recurrence in Portugal. The study concerns the period 2002–2009 and, although the situation may have changed over the last decade, this cannot be assessed unless datasets linking multiple disease episodes at the individual level are made available to researchers. Understanding risk factors for TB recurrence in Portugal can help to define new guidelines to reduce the prevalence of recurrence, decreasing the chance of multi-drug resistant TB development.

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Diagnostic challenges of hypersensitivity pneumonitis with autoimmune features: Dealing with more than a coincidence?



To the Editor,

Besides the well-known relationship between connective tissue diseases (CTDs) and several forms of interstitial lung disease (ILD), the recognition of autoimmune features in idiopathic interstitial pneumonias led to the establishment of the IPAF (interstitial pneumonia with autoimmune features) denomination and classification criteria in 2015.¹

Hypersensitivity pneumonitis (HP) and several CTDs share T cell dysregulation, suggesting a greater likelihood of autoimmune disease in HP patients. A previous study of a cohort of chronic, fibrotic HP patients found that fifteen percent of these patients revealed either the presence of a defined CTD or some autoimmune features suggestive of CTD. These patients were identified as having “HP with autoimmune features” (HPAF) and seemed to have a worse survival rate than non-HPAF HP patients.²

We report a case of a 72-year old man who is followed as a Pulmonology outpatient due to obstructive sleep apnea syndrome, under home continuous positive airway pressure

(CPAP) therapy, chronic obstructive pulmonary disease with mild centrilobular emphysema and mediastinal lymph node enlargement. Inhalation exposure is relevant due to former smoking habits (thirty pack-years), close contact with birds in the backyard, occasional use of sauna and Turkish Baths. As for past medical history, the patient also has arterial hypertension, dyslipidemia, unknown chronic liver disease and a previous rheumatological diagnosis of psoriatic arthritis, currently without directed therapy; a previous hospital admission happened due to community-acquired pneumonia. Chronic medications are an association of two anti-hypertensive drugs and atorvastatin.

Follow-up chest high-resolution CT scans showed progressive, unspecific, peripheral lower lung lobes intralobular reticulation (Fig. 1), as well as lymph node enlargement (14mm) in the left paratracheal station (4L). Endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) was performed; the 4L station was identified and sampled and its cytological analysis was unremarkable.

Meanwhile, the patient reported worsening exertional dyspnea. Body plethysmography identified a mild obstructive ventilatory defect: FEV1/VC ratio equal to 64.2% and FEV1 equal to 2.41 L (86% of the predicted value). There was no lung diffusion impairment. Fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) in the middle