ABSTRACT

Despite all scientific progress, tuberculosis remains as the leading cause of death from a curable infectious disease. Drug-resistant tuberculosis is a major threat to disease control and constitutes an important public health problem.

In 2010, the World Health Organization estimated the existence of 650,000 cases of multidrug-resistant tuberculosis (MDR-TB) worldwide. Such patients are resistant to the most effective anti-tuberculosis drugs: isoniazid and rifampicin.

In Europe in 2009, 14.6% of patients were resistant to one or more first-line anti-tuberculosis drugs (rifampicin, isoniazid, ethambutol and streptomycin) and MDR-TB patients constituted 5.3% of all registered cases of tuberculosis.

In Portugal, the proportion of patients resistant to one or more first-line anti-tuberculosis drugs was 13.8% of all tuberculosis cases registered in 2009. In the same year, the overall proportion of MDR-TB was 1.5%. Although the proportion of MDR-TB is comparable with the median incidence in Europe, the proportion of the most severe form of resistance (extensively drug-resistant tuberculosis) is high in Portugal (32%) when compared with the proportion in Europe (7%).

International studies have identified various risk factors for drug-resistant tuberculosis. Epidemiological studies conducted so far concluded that inadequate or poorly administered treatment regimens are important risk factors for drug resistance but results are not consistent for individual characteristics that may enhance the occurrence of resistance.

Although in Portugal resistance to anti-tuberculosis drugs is a National tuberculosis Control Program priority, very few studies have focused on the relevant risk factors. The characteristics of each country may influence the occurrence of drug-resistant tuberculosis. Therefore, the knowledge of risk factors is essential to prevent the resistance.

The aim of the present dissertation was to identify risk factors for drug-resistant tuberculosis in northern Portugal, through the accomplishment of the following specific objectives:

1. Characterize the drug-resistant tuberculosis in the north of Portugal;
2. To analyze the relationship between risk factors and resistance to first line anti-tuberculosis drugs.

**Article: Risk factors for drug-resistant tuberculosis in northern Portugal**

This report comprises a retrospective case-control study. The medical records and drug susceptibility test data from tuberculosis patients diagnosed between 31 March 2009 and 1 April 2010 were examined. The study enrolled 119 patients with any drug resistance to first line anti-TB drugs (cases) and 238 with drug-susceptible TB (controls). Each case was matched with two control according age group.

Cases and suitable controls were identified by consulting the regional drug susceptibility test database. All randomly selected controls had already concluded the treatment. Demographic characteristics and risk factor information were routinely obtained from each patient on admission to a Tuberculosis Unit. This information was collected using a structured questionnaire and stored in the National Tuberculosis Surveillance System (SVIG-TB).

The measure of association between drug resistance and each potential risk factor was reported by odds ratio (OR) and the 95% confidence intervals (95% CI) using conditional logistic regression models.

The investigation revealed that during the study period, 14.6% of all tuberculosis cases registered in northern Portugal was resistant to one or more first line anti-tuberculosis drugs and 8.4% had MDR-TB. The results of the study showed that there were risk factors for drug-resistant tuberculosis the intravenous drug use (adjusted OR 4.77; 95% CI: 1.24-18.32), presence of diabetes mellitus (OR: 3.54; 95% CI: 1.45-8.66) and previous tuberculosis treatment (OR: 2.48; 95 %CI: 1.12-5.49).

Identifying clinical predictors of drug resistance can allow risk patients identification and subsequent reinforcement of treatment supervision. Therefore, the knowledge of risk factors for drug resistance is an important tool to prevent future cases and disease control.