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ABSTRACT OF PhD THESIS

Improving early diagnosis and adherence to treatment in patients with pulmonary and extrapulmonary tuberculosis in Mureș County

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Introduction. Tuberculosis (TB) is an infectious-contagious disease widespread worldwide, which associates significant morbidity, disabling complications, and high economic-social costs. Increased mortality makes TB one of the top 10 causes of death worldwide. The incidence of the disease at the national level (37.3‰) and in Mureș County (24.5‰) is far above the European average (7.3‰). TB represents a significant public health problem and requires increased attention from doctors of all specialties for early diagnosis and correct treatment. TB control involves special efforts: investigations to confirm the disease and differential diagnosis, permanently supervised treatment for lasting cure with avoidance of chronicity, and prophylactic measures to prevent the spread of the disease.

Objectives. The objectives of this study consist in the dynamic characterization of the TB endemic in Mureș County, the identification of avoidable TB risk factors, the evaluation of chemoresistance to antituberculosis drugs and special categories such as cases of extrapulmonary TB (EPTB) and those with co- TB-HIV/AIDS infection. We assessed the influence of the COVID-19 pandemic on the TB pandemic. Other objectives aimed to evaluate the contribution of "Polymerase Chain Reaction - GeneXpert" genetic methods in the early diagnosing of severe paucibacillary TB and demonstrate the usefulness of targeted TB screening in high-risk individuals. The work carried out a multidirectional approach to TB, focused on the assessment of risk factors, means of confirmation, and increasing patient compliance to prevent complications and disease transmission.

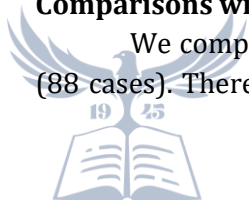
Study I: Analysis of diagnosis and treatment in patients with tuberculosis from Mureș county in 2020–2022. Comparisons with the years 2017-2019.

Study I includes subgroup I - 526 patients with active TB in Mureș county in 2020-2022 and subgroup II - 798 patients with active TB from 2017-2019. Pulmonary and extrapulmonary TB has shown a significant decrease in the last three years due to the intensification of the anti-tuberculosis fight and due to the isolation measures imposed by the COVID-19 pandemic. We identified the main risk factors of the disease: male gender, young-average age, rural origin, active smoking, alcohol consumption, lack of occupation and stable income, living conditions, and poor schooling.

Suggestive symptoms of TB (statistically significant) were hacking cough and bacillary impregnation syndrome. All patients benefited from radiological investigations, and in the presence of suggestive changes, we performed specific bacteriological examinations of different biological products. The overall confirmation rate was 80.95%, above the European average. 421 GeneXpert investigations were performed on microscopically negative cases and in EPTB with a positivity rate of 14%, thus gaining 21-60 days, allowing the rapid introduction of treatment. We diagnosed cases of rifampicin resistance, allowing the early introduction of individualized therapy and eliminating failures and secondary chemoresistance. All patients benefited from antibiotic treatment, the evolution being favorable in 80% of cases. Compliance was low (60.3-73.3%), and the fatality rate was high (8.68%). We identified 46 cases of chemoresistance (3.46%), with a significant decrease in recent years, 30.43% being multidrug-resistant. Patients had multiple comorbidities and require prolonged treatment with backup drugs. The therapeutic success rate was low (56.5%), and the fatality was high (13%) compared to TB with susceptible germs.

Study II: Extrapulmonary tuberculosis in Mureș county during 2020-2022. Comparisons with the years 2017–2019.

We compared two subgroups of EPTB patients from 2020-2022 (39 cases) and 2017-2019 (88 cases). There was a significant decrease in the dynamics of cases. Pleural, osteoarticular, and



lymph node TB predominated. The overall confirmation rate was 64.56% with laborious investigations. In cases without bacteriological confirmation, a multidisciplinary team corroborated the epidemiological criteria, immunosuppressive risk factors, clinical symptoms, and the result of paraclinical studies. All patients benefited from prolonged antituberculosis treatment and surgical treatment if it was necessary. Overall compliance was low, and fatality increased (from 4.54% to 17.94%).

Study III: Association of tuberculosis with HIV infection or AIDS disease in Mureș county. Comparison of data recorded from 2014-2022 with 2004-2013.

Subgroup I included 52 patients with TB-HIV co-infection from 2014-2022, and subgroup II 70 patients from 2004-2013. We observed reduced cases (through intensification of antiretroviral treatment and active screening) and an increase in the average age. The patients were mainly in the AIDS stage, associated with multiple opportunistic infections and a high frequency of EPTB. Drug chemoresistance, treatment failures, and dropout were more common than in TB and HIV-negative patients. The fatality is significantly decreasing.

Study IV: Early diagnosis in contacts of TB patients. Active screening in the population at high risk of TB in Mureș county during 2020-2022.

We examined 2038 people at the highest risk for TB, contacts of the 526 patients taken into active TB records in 2020-2022 in Mureș County. Contacts benefited from clinical examination, IDR2PPD (in children), radiological investigations, bacteriological examinations (conventional and GeneXpert), and specialist consultations in EPTB. A statistically significant number of TB cases - latent infection (158) that benefited from chemoprophylaxis and 35 cases of active TB that entered the complex TB treatment program were detected.

Conclusions (general).

The TB endemic in Mureș County remains high, with lower incidences than the national one. If detected early, the identified risk and prognostic factors, together with clinical thinking and targeted investigations, can lead to improved diagnosis and treatment of TB. Improving living conditions, employment and the intensification of education through schooling can represent basic foundations in decreasing TB endemicity.

Chest X-ray was an indispensable investigation in the diagnosis of TB. Bacteriological confirmation was superior to bacteriological confirmation found in European studies. The GeneXpert test increased rapid confirmation and allowed the introduction of treatment in severe forms. The high endemicity of TB implies the need to expand the genetic method of germ identification and antibiogram. Chemoresistance is still essential and is associated with severe cases, a high rate of failure, and death. Through interdisciplinary collaborations, active detection can be optimized by periodic clinical-radiological evaluation of people at high risk of TB.

TB etiology will always be considered in trailing extrapulmonary involvement with increasing bacteriological/histopathological confirmation in regions with still high endemicity. HIV testing of all TB patients and active TB screening in all HIV-positive patients is essential to improve the detection of TB-HIV co-infection. The general increase in patient compliance to investigations/treatment during the contagious period becomes a primary objective. It requires targeted measures of education and optimization of accessibility to controls, specialized medical staff in sufficient numbers, accessible means of transport for the sick, and adequate social assistance. Early detection of TB at symptomatic or through active screening, prolonged isolation, and supervised treatment control can prevent transmission of infection, failures, and chemoresistance and, over time, lead to a significant decrease in TB endemicity.