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## Original Research Article

# Factors associated with sputum culture conversion in patients with pulmonary tuberculosis

Greta Musteikienė<sup>a,\*</sup>, Skaidrius Miliauskas<sup>a</sup>, Jurgita Zaveckienė<sup>b</sup>, Marius Žemaitis<sup>a</sup>,  
Astra Vitkauskienė<sup>c</sup>

<sup>a</sup> Department of Pulmonology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>b</sup> Department of Radiology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>c</sup> Department of Laboratory Medicine, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

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## ABSTRACT

**Objective:** The aim of this study was to determine what factors are associated with sputum culture conversion after 1 month of tuberculosis (TB) treatment.

**Materials and methods:** A total of 52 patients with new drug susceptible pulmonary TB were included in the study. Patients completed St. George respiratory questionnaire (SGRQ), they were asked about smoking, alcohol use, living conditions and education. Body mass index (BMI) measurements, laboratory tests (C reactive protein [CRP], vitamin D, albumin) were performed, and chest X-ray was done. After 1 month of treatment sputum culture was repeated.

**Results:** Culture conversion after 1 month of treatment was found in 38.5% cases. None of investigated social factors appeared to have an effect on conversion, but worse overall health status (as reported in SGRQ) and longer duration of tobacco smoking were detected in the “no conversion” group. Concentrations of albumin, CRP, X-ray score and the time it took *Mycobacterium tuberculosis* culture to grow also differed. Patients who scored 30 or more on SGRQ were more than 7 times as likely to have no conversion. However, the most important factor predicting sputum culture conversion was sputum smear grade at the beginning of treatment: patients with grade of 2+ or more had more than 20-fold higher relative risk for no conversion. Using receiver operating characteristic curve analysis, we also developed a risk score for no conversion.

**Conclusions:** The most important factors in predicting sputum culture conversion after 1 month of treatment were grades of acid-fast bacilli in sputum smears at time of diagnosis and scores of SGRQ.

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\* Corresponding author at: Department of Pulmonology, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50161 Kaunas, Lithuania.

E-mail address: [greta.musteikiene@gmail.com](mailto:greta.musteikiene@gmail.com) (G. Musteikienė).

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## 1. Introduction

According to European Centre for Disease Prevention and Control (ECDC) Lithuania is still a high tuberculosis (TB) priority country [1] and, although the prevalence of TB is slowly decreasing, in 2015 there were still 41.89 new TB cases per 100 000 population [2]. Among those 11.5% were multi drug-resistant TB (MDR-TB) [2]. The prevalence of human immunodeficiency virus (HIV) infection in Lithuania was 4.8 per 100 000 population (2014) [3] and the main AIDS-defining illness was TB [4].

It is well known that TB is not only a medical condition but also a social problem. Patients diagnosed with TB are contagious and, at least at the beginning of treatment, are kept in hospitals where they are separated from their family, work and social life. It is a national policy to keep patients isolated until they become culture negative.

In the national guidelines [5] it is recommended that sputum smears and culture should be repeated after two months of treatment. Sputum smear conversion at this time is believed to be one of the best biomarkers for prognosis of treatment success without the probability of relapse in the future [6–8]. However, two months of isolation in hospital can make a significant impact on professional or personal life of a TB patient.

According to the previously published studies, the presence of cavitory TB disease appears to be associated with an increased time to sputum smear conversion [9]. It is assumed that cavitation is related to a higher grade of bacteria in the lungs. Other studies also found different factors that are associated with sputum culture conversion. It was shown that culture conversion could be influenced by history of smoking [10], body mass index (BMI) [11], sputum smear grade before the treatment [12], vitamin D concentration [13], albumin concentration [14] and various social factors [15].

In this study we performed the microbiological testing after 1 month of treatment and aimed to determine what factors were associated with faster sputum culture conversion in cases of pulmonary TB.

## 2. Materials and methods

The study was carried out in one of the largest TB hospitals in Lithuania. Approximately 95% of patients treated here are from Kaunas district, which is the second largest district in Lithuania and constitutes around 12.4% of Lithuania's territory and 20% of population. Only adults are treated in our hospital and directly observed treatment (DOT) is fully implemented as the staff ensures that patients are taking their medication seven days a week.

From November 2015 all patients with first-time diagnosis of pulmonary TB, meeting no exclusion criteria (significant morbidity due to other illnesses (e.g. cancer, autoimmune diseases, renal insufficiency); HIV positive; pregnant or breastfeeding) were asked to participate in this clinical trial. We selected these exclusion criteria to avoid the variability of laboratory tests and radiological changes, caused or influenced by other diseases, except TB. There were no patients with

diabetes mellitus in our study group. During the period of one year (up to November 2016) 96 patients were included in the study, and 52 of them with drug susceptible pulmonary TB were analyzed in this article. Upon inclusion, acid-fast bacilli (AFB) had to be found in sputum with Ziehl–Nielsen histochemical reaction or positive *Mycobacterium tuberculosis* culture in MGIT BACTEC had to be detected. Selection process can be seen in Fig. 1. Two of sputum smear positive patients later were confirmed to have atypical mycobacteriosis and were excluded from the study. All patients in this study, eventually were bacteriologically confirmed to be infected with *M. tuberculosis* on MGIT BACTEC culture.

Quality control of smear microscopy was performed by the Central Tuberculosis Reference Laboratory. AFB smear positive results were as per World Health Organization/International Union Against Tuberculosis and Lung Disease grading: “scanty” with of 1–9 AFB per 100 oil immersion fields; “1+” with 10–99 AFB per 100 oil immersion fields; “2+” with 1–10 AFB per 1 oil immersion field and “3+” with >10 AFB per oil immersion field. All TB patients were offered rapid HIV testing foreseen in the National guidelines [3,5]. None declined to be tested. If patient was found to be HIV positive, he/she was excluded from the trial.

Before the initiation of the TB treatment postero-anterior chest X-ray was done, patients completed St. George respiratory questionnaire (SGRQ) and answered the question about their overall health status (multiple-choice question with 5 possible answers: “very good”, “good”, “average”, “bad”, and “very bad”) in the Lithuanian (native) language, they were asked about smoking habits, alcohol use, occupation, living conditions (rural or urban residence; family status) and education. The result of SGRQ was calculated using a program provided by St George's University of London. Body mass index (BMI) measurement, and laboratory tests from peripheral blood (C reactive protein (CRP), vitamin D, and albumin) were performed before the start of TB treatment. Pack-years of cigarette smoking were calculated based on the interview with a patient (by multiplying the number of packs of cigarettes smoked per day by the number of years the person has been smoking). Chest X-ray was evaluated by an experienced radiologist and the score of disease spread was calculated according to the method described by Ralph et al.: presence of baseline cavitation and the total percentage of lung affected were recorded and a score was calculated (CXR score = proportion of total lung affected (%) + 40 if cavitation is present) [16]. CRP, albumin and vitamin D testing was performed at the hospital of Lithuanian University of Health Sciences Kaunas Clinics, an externally quality-assured laboratory. We defined vitamin D values 70–250 nmol/L as optimal; 51–69 nmol/L, as insufficient, and below 50 nmol/L, as deficient. Reference values for CRP were 0–7.5 mg/L and for albumin, 35–48 g/L.

After 1 month of in-hospital DOT, sputum microscopy, sputum culture and CRP were repeated.

Statistical analysis was performed using SPSS version 23.0 for Windows (Statistical Package for the Social Sciences, Chicago, IL, USA). The following descriptive statistics were reported: proportions with their 95% confidence intervals for dichotomous variables and medians with their interquartile ranges (IQR) for continuous variables. Categorical variables were evaluated using the Pearson  $\chi^2$  test. Comparisons of

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