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## Abstract

**Background**: In pulmonary tuberculosis (PTB), the sputum conversion rate at 2 months is frequently used to evaluate treatment outcomes and effectiveness of a TB control programme.

**Aims**: The study aimed to estimate the rate of delayed sputum conversion and explore its predicting factors at the end of the intensive phase among smear-positive PTB (PTB +ve) patients.

**Methods**: A 3-year retrospective study was conducted in the government hospital in Pulau Pinang from 2016 to 2018. During the study, a standardized, data collection form was used to collect data from the patient record. Patients aged over 18 years were recruited. Multivariable logistic regression analysis was used to identify significant independent variables associated with delayed sputum conversion.

**Results**: A total 1128 of PTB patients were recorded visiting the TB clinic, 736 (65.2%) were diagnosed as PTB +ve; of these, 606 (82.3%) PTB +ve had a record of sputum conversion at the end of the intensive phase. Age ≥ 50 years, blue-collar jobs, smoking, heavy bacillary load, relapsed and treatment interrupted were significantly (P

**Conclusion**: The rate of sputum smear conversion in the intensive phase of treatment was independently associated with high sputum smear grading at diagnosis, relapsed and treatment interrupted categories, old age and blue-collar occupations.

Keywords: delayed conversion rate, tuberculosis, sputum, bacillary count, treatment outcomes

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## Introduction

Sputum smear conversion from positive to negative is one of the useful indicators to determine the efficacy of anti-tuberculosis treatment and essential in the clinical evaluation of patients with smear-positive pulmonary tuberculosis (PTB +ve). Delayed sputum smear conversion after 2 months of intensive phase has been associated with possible continuity of infectiousness, higher risk of treatment default, treatment failure, development of drug-resistant tuberculosis (TB) and the potential increase in TB mortality (1). The sputum smear conversion rate is defined as the percentage of registered smear positive TB cases in a given period converting to smear negative after 2 months of anti-tuberculosis treatment (2,3). The World Health Organization (WHO) recommends an annual assessment of treatment outcomes to identify risk and create policies to improve the efficiency of national TB control plans.

The most effective way of preventing the transmission of TB is the identification and cure of infectious

PTB +ve patients (4). Active PTB and PTB +ve with a heavy bacillary load are the primary sources of infection (5) besides having the capacity of transmitting TB to 15 people a year (6). According to WHO, all PTB +ve patients should be evaluated for bacteriological status after the intensive phase to determine treatment outcomes (7).

In Malaysia, TB is a significant health problem with the current incidence rate of 92 per 100 000 and an annual mortality rate of 4.1 per 100 000 population (7). Malaysia is a multi-racial country with 3 different main ethnic groups: 67.4% Malay, 24.6% Chinese and 7.3% Indian, 0.7% other (8). The TB control programme encompasses various indicators to examine TB prevention and control. For the past 5 years, the sputum conversion rate was reported in the range of 60–80% and the treatment success rate 75–78%, despite the 85% TB treatment success rate defined by the WHO global target (1,9). Therefore, evaluating risk factors for delayed sputum conversion is necessary for health care providers and policy-makers to ensure the correct measures to avoid unfavourable outcomes. Factors affecting sputum smear conversion have previously been studied in Malaysia (1,10–12) and some research has discussed treatment outcomes of TB therapy (9). The present study is different from previous studies (conducted in Malaysia) in evaluating the trends of PTB over the past 3 years, estimating the rate of delayed sputum conversion, and exploring its predicting factors together with the association of delayed sputum conversion rate with treatment outcomes among PTB +ve patients. Hence, the objective of the current study is to determine the sputum conversion rate and identify the risk factors of delayed sputum conversion at the end of the intensive phase of treatment.

## Methods

### Study design and settings

We conducted a retrospective study of PTB +ve patients registered from 2016 to 2018 in Pulau Pinang hospital, a tertiary care public hospital with 1017 beds situated in northern Malaysia. Tuberculosis-related information was indexed and analysed using hospital case records of patients over 18 years old with all comorbid conditions.

### Data collection

A data collection form was specially designed for this study and all data information was transferred on it from the patient record file. The main variables of data tool were sociodemographics, clinical presentation of TB, bacteriological examination during management, patient's previous medical record, duration of therapy, and treatment outcomes. We retrospectively reviewed all PTB +ve patients who visited or were transferred in and diagnosed with confirmed bacteriological and radiological evidence of PTB.

### Diagnosis

Initial TB diagnosis is based on bacteriological results of sputum smear examination of acid-fast bacilli (AFB), (Xpert MTB/RIF assay, Cepheid, New Jersey), sputum culture, chest X-ray, and histopathology examination of any tissue in the case of extra-pulmonary TB. Sputum samples are collected from each patient over 2 or 3 consecutive days and sent to a local laboratory for microscopic examination. For PTB +ve patients, the Xpert MTB/RIF assay is used as an add-on

diagnostic to detect rifampin-resistant strains and bronchoalveolar lavage for patients who are unable to expectorate sputum. Laboratory tests, including full blood count, liver function test, blood glucose level, human immunodeficiency virus (HIV) screening and erythrocyte sedimentation rate are carried out on diagnosis. Posteroanterior chest X-rays are performed for all patients before treatment, at the end of the intensive phase and at the end of TB treatment. The severity of disease is measured by the number of lobes and the presence of cavitation (2).

PTB+ve patients with at least 2 initial sputum smear examinations positive for AFB or one sputum smear examination positive with radiological abnormality or sputum culture positive for mycobacterium TB were receiving a standard 6-month course of antituberculosis treatment. First, 2 months of intensive treatment have fixed-dose combination tablets containing rifampicin (600 mg), isoniazid (300 mg), pyrazinamide (1500 mg), and ethambutol (1200 mg). This is followed by a 4-month continuous phase with a daily dose of isoniazid and rifampicin. Patients who remained smear positive even after the intensive phase or who had cavitary disease received more extended treatment with the first-line anti-tuberculosis treatment continuing till the end of the 3rd month. Treatment outcomes in Malaysian guidelines are defined as per WHO recommendations (Table 1) (13).

Cured and treatment complete were represented as TB treatment success; treatment failure, died and transferred were classified as unsuccessful treatment outcome. Sputum grading is categorized according to the current number of AFB at the time of sputum smear microscopy after scanning using the Ziehl–Neelsen technique. The WHO recommends 4 grades of PTB +ve cases: scanty (1–9 AFB/100 fields), 1+ (10–99 AFB/100 fields), 2+ (1–9 AFB/50 fields), and 3+ (> 10 AFB/field in at least 20 fields) (14).

**Data analysis**

Data were analysed using SPSS. The Pearson chi-squared test was used for categorical variables to make a comparison of proportions. Multivariable logistic regression analysis was used to examine the possible association between a dependent variable and independent risk factors for delayed bacteriological conversion at the end to the intensive phase of TB management. P-value