Effect of cigarette smoking on sputum smear conversion time among adult new pulmonary tuberculosis patients: A study from Iran Southeast

Maliheh Metanat, Batool Sharifi-Mood[*]**, Mina Parsi, Sara Sanei-Moghaddam**
Research Center for Infectious Diseases and Tropical Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

ABSTRACT

Background: Cigarettes smoking is a risk factor for tuberculosis (TB). Associations between smoking and TB disease have been reported, but there are few reports on the influence of smoking on the sputum smear and culture conversion time. This study surveyed the possible association between smoking and sputum smear conversion time among new smear-positive pulmonary tuberculosis patients.

Patients and methods: Between May 2005 and December 2006, we evaluated smokers and non-smokers patients with pulmonary TB referred to Zahedan Tuberculosis Center (Southeastern Iran). Patients were not immunosuppressed or infected by human immunodeficiency virus (HIV). Drug resistant cases were also excluded.

Results: A total of 200 TB patients, including 100 smokers, were evaluated. There was a significant delay in sputum smear conversion time between smokers and non-smokers 2 (53% vs. 10%, respectively, $p<0.001$) and 3 months following the treatment (19% vs. 2%, respectively, $p<0.001$). However, there was no significant difference in failure rate (a positive smear at the end of the 5th month of treatment) between two groups (95% vs. 97%).

Conclusion: Our results revealed that smoking is significantly associated with a delay in sputum smear conversion time, hence, pulmonary TB cases must be strongly encouraged to cease smoking.

Keywords: *Cigarette smoking, Pulmonary tuberculosis, Treatment, Sputum smear conversion time.*
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INTRODUCTION

Tobacco smoke contains large quantities of toxic chemicals. Chemical analysis shows the tobacco is composed of an unusual number of constituents including nicotine, nicotianine, and tobacco, malic , sulphuric, phosphoric, citric, acetic acids (1). Discussion of the association between tobacco consumption and tuberculosis (TB) has a long history. Since 1918, the association between

tuberculosis and smoking has been investigated (2). Evidence indicates that smoking (both current and former, passive and active) is associated with increased risk of being infected with *Mycobacterium tuberculosis*, developing more severe TB, and risk of dying of TB (1-4). Understanding the impact of smoking on TB outcomes is critically important if we want to control TB. Smoking damages the lung's defense mechanism against infections including chronic TB and other infections (5,6). The alveolar macrophage is the first cell to ingest a tubercle

bacillus following infection (4,5). Cigarette smoke activates alveolar macrophages to produce a local inflammatory response, but nicotine suppresses the antigen presentation function to develop a specific immune response and induces T cell anergy (4-7). Natural killer cell activity is also less and significantly suppressed in smokers. Interleukin-18 is reduced in induced sputum from smokers (5-8). Therefore, chronic exposure to cigarette smoke reduces T cell immunity. Since there is such immunodeficiency pattern in smokers, clinical manifestation, imaging test and response to treatment can be different with non-smokers.

Previous studies have shown the association between cigarette smoking and tuberculosis (9-14). However, there is not any study in Sistan and Baluchestan province, where the incidence of tuberculosis and rate of addiction is high (15). Therefore, we decided to evaluate the association between cigarette smoking and smear conversion time among new smear-positive pulmonary tuberculosis patients.

PATIENTS and METHODS

In this case-control study, we evaluated 200 consecutive smear-positive pulmonary TB patients (including 100 smokers and 100 non-smokers) referred to Zahedan Tuberculosis Center. The following inclusion criteria were applied at baseline: new case, smear positive pulmonary TB, aged more than 18 years, no malignant disease or immunodeficiency condition like diabetes, or other underlying disease, and Iranian race. Informed consent was obtained and the study protocol was approved in the Ethical Committee of Zahedan University of Medical Sciences.

Smoking was defined as having ever smoked, even one cigarette per day for at least one year. Current smoker was defined as sometimes or daily smoker, while ex-smoker was a person who has smoked for at least one year but ceased smoking at the time of study. The average number of cigarettes smoked per day was recorded for all ex-smokers and current smokers. All patients treated according to national guideline. The treatment regimen for all adults with previously untreated tuberculosis should consist of a 2-month initial phase of isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) and continued for another four months with INH and RIF. Monitoring and response to treatment was checked by sputum smear, but not culture (according to national program), at the end of the 2nd and 3rd months of treatment and then at the end of the 5th month of treatment course. Failure was defined as a patient who had a positive sputum smear at the end of the 5th month of treatment.

Finally, all demographic, clinical, radiological and laboratory results in two groups were reviewed and compared. Statistical analysis was performed using SPSS software (version 11.0, SPSS Inc., USA). Data were analyzed by chi-square test and $p<0.05$ was considered significant.

RESULTS

Two hundred TB patients (119 males) with a mean age of 32.0 ± 11.4 years old were enrolled. There was no significant difference in age between smokers and non-smokers ($p=0.34$), however, the difference was significant in sex where 16 smokers and 65 non-smokers were female and 94 smokers and 25 non–smokers were male ($p<0.05$).

Totally, 63% of smokers had a history of chronic cough (cough for more than 3 weeks) due to chronic bronchitis. Smokers suffered from their initial symptoms during the past 4 to 7 months. Meanwhile, 16% of female and 44% of male smokers had persistent cough and dyspnea after the treatment. Following the treatment 84% of smoker females and 56% of smoker males cured. These figures were 92% and 88% among non-smoker females and males, respectively.

Radiographically, smokers with pulmonary tuberculosis (PTB) presented with cavitation (22% vs. 17%), miliary lesions (17% vs. 11%), multiple

nodules or masses (21% vs. 13%), and infiltrations in two lungs (29% vs. 21%) more commonly than never-smokers.

There was a significant delay in sputum smear conversion time, when smokers and non-smokers were compared at the end of the 2nd (53% vs. 10%, p<0.001) and 3rd month of treatment (19% vs. 2%, p<0.001) (table 1). Moreover, there was a significant difference in sputum smear conversion time between heavy smokers (15-20 cigarette/day) and those smoked 10-15 cigarette/day (p<0.05). This significant difference was also found between those smoked 5-10 cigarette/day and patients who smoked <5 cigarette/day. Finally, all patients including smokers and non-smokers received a full course of treatment and there was no significant differences in failure rate (a positive smear at the end of the 5th month of treatment) between two groups (95% vs. 97%).

Table 1. Sputum smear results at the end of the 2nd and 3rd months of treatment in smokers and non-smokers according to sex

	Sputum smear result			
	2nd month		3rd month	
	Pos.	Neg.	Pos.	Neg.
Smoker women	9(56.3)	7(43.7)	3(18.8)	13(71.2)
Non-Smoker women	2(3.1)	63(96.9)	0	65(100)
Smoker men	50(53.2)	44(46.8)	18(19.1)	76(80.9)
Non-Smoker men	7(28.0)	18(72.0)	2(8.0)	23(92.0)

Pos.: positive; **Neg.**: negative

DISCUSSION

Sputum smear and culture conversion are important indicators for the effectiveness of treatment and the infectivity of the patient with TB (16). For hospitalized patients with smear-positive pulmonary or laryngeal tuberculosis, the Centers for Disease Control and Prevention recommends that three consecutive sputum samples be negative for acid-fast bacilli (AFB) before respiratory isolation is discontinued (17). In Iran, since sputum culture is not routinely achieved in TB centers, sputum smear conversion is an indicator for

monitoring and effectiveness of treatment in TB Centers. Our study identified that cigarette smoking is an important factor influencing sputum smear conversion time among new cases of pulmonary tuberculosis. We observed that 53% of smoker patients and 10% of non-smokers had a positive sputum smear at the end of the 2nd month of treatment. Meanwhile, at the end of the 3rd month, 19% of smokers had still a positive sputum smear. It is expected that at the end of the 2nd month of treatment in four-drug regimen, sputum conversion occurs in 85-90% of patients and at the end of the 3rd months only 3-5% had a positive sputum smear. Hence, smoking was found to be significantly associated with a delay in sputum smear conversion time. In a study in India, smokers were four times as likely to die from tuberculosis as non-smokers (12).

Tuberculosis can sometimes stay in a person's lungs for a long time without making him sick. This is called latent TB. Smoking can cause latent TB to become active. If a person is being treated for TB, smoking will also make the treatment take longer (12). Similarly to ours, Guler et al claimed that smoking was significantly associated with a delay in sputum smear conversion time. In their study, smoking was a factor associated with persistent sputum smear and culture positivity at the end of the 2nd month of treatment (16). Kollapan study showed that there was an association between tobacco smoking and the development of PTB which is dose dependent (12). In another study, there was a dose-response relationship between the number of cigarettes smoked daily and the risk of active (bacillary) PTB (13).

Ariyothai and colleagues found that the effects of passive smoking in the office and/or neighborhood on PTB were strong. Persons with such exposures had a higher risk of PTB than no exposure or exposure ≤3 times/week (14). All these reports show that nicotine could not only be responsible for the higher incidence of TB in

smokers, but also be significantly associated with a delay in sputum smear conversion time. Smoking also can contribute to other diseases, such as respiratory bronchiolitis, obstructive sleep apnea, idiopathic pneumothorax and pulmonary cancer (12,13,16,17).

In conclusion, upon the results emerged from our study, there is an association between cigarette smoking and a delay in sputum smear conversion time in new cases of PTB.

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