

Time to Sputum Smear Conversion in Smear-Positive Pulmonary Tuberculosis Patients and Factors for Delayed Conversion

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What's Known

- Sputum smear negativity is a sign that indicates the response to anti-tuberculosis treatment.
- There is currently limited data available from developing countries like Iran, regarding the time required for sputum smear conversion in patients who take anti-tuberculosis. This is particularly the case in eastern Iran due to the migration of people from Afghanistan and the probable emergence of drug resistant cases.

What's New

- We conducted this study to estimate sputum AFB smear conversion rate and associated risk factors delaying sputum AFB smear conversion.
- Mature male patients with pre-existing illness, bacilli density in initial smear, and severe involvement of the lung on radiography need to be monitored more closely.
- Based on the study outcome, we can propose policies for treatment and follow up of tuberculosis in Iran.

Abstract

Pulmonary tuberculosis is a common infection worldwide. In the eastern part of Iran, fluctuations in tuberculosis prevalence are seen due to the migration of people from Afghanistan. The aim of this study was to evaluate the time of bacteriologic sputum conversion after treatment and affecting factors in those whose smear does not become negative. This study was carried out on 85 smear-positive pulmonary tuberculosis patients with the mean age of 65.6 ± 16.7 years. There were 38 male patients (44.7%), 47 urban residents (55.3%), and only 6 patients (7.1%) from Afghanistan. The mean time of sputum conversion after starting treatment was 1.99 ± 1.06 months. The mean time of sputum conversion was significantly higher in males ($P=0.046$), increased bacilli density in the primary sputum sample ($P<0.0001$, $R=0.507$), and pre-existing medical illness ($P=0.001$). In this study, it was revealed that pre-existing illness, bacilli density in initial smear, and severe involvement of the lung on radiography, could be associated with delay in sputum smear conversion.

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Keywords • Radiography • Sputum • Pulmonary tuberculosis • Bacteriologic conversion

Introduction

Pulmonary tuberculosis is a common infection worldwide.¹ In Iran, particularly in the eastern part, fluctuations in tuberculosis prevalence are seen due to the migration of people from Afghanistan.² In smear-positive pulmonary tuberculosis, bacteriological study is a superior method in following the response to treatment.³ Currently, the follow-ups are performed at the end of months 2, 4, and 6 via sputum smear study looking for acid-fast bacilli (AFB). In patients whose sputum smear does not become negative after the fifth month of treatment, treatment failure is suggested.²

Some factors may affect the time of sputum smear conversion.^{4,5} The aim of this study is to evaluate the time of sputum smear conversion after treatment initiation and to study possible affecting factors in those whose smear does not become negative.

Materials and Methods

This prospective (descriptive-analytic) study was carried out on all pulmonary tuberculosis patients who attended Birjand Tuberculosis Center during 2010-2011. The diagnostic criteria for pulmonary tuberculosis were at least two positive sputum smears, or a positive sputum smear and a suspicious radiography, or a positive smear along with a positive culture. The exclusion criteria were drug resistant, relapse cases and patients with HIV infection, death during treatment, inability to collect sputum, and transfer to other institutions.

Prior to participation, a questionnaire was filled out for each patient containing demographic information, pre-existing medical illness (diabetes, cancer, heart disease, etc.) and COPD, the time of pulmonary tuberculosis diagnosis, treatment initiation time, and the number of live bacilli in sputum sample before the treatment followed by 1, 2, 3, 4, 5, and 6 months after treatment. The time of sputum smear conversion was recorded for each patient considering the treatment initiation time. Collected data were analyzed using the SPSS software (version 15.0).

Results

This study was performed on 85 smear-positive pulmonary tuberculosis patients with the mean age of 65.6 ± 16.7 years, ranging from 15 to 93. There were 38 male patients (44.7%), 47 urban residents (55.3%), and only 6 patients (7.1%) from Afghanistan.

Regarding primary bacilli density before treatment, 25 patients (29.4%) were 1+, 21 patients (24.7%) were 2+, and others (45.9%) were 3+. The mean time of sputum conversion after starting treatment was 1.99 ± 1.06 months. The mean time of sputum conversion was significantly higher in males compared with females. This time was also prolonged in those with pre-existing medical illness in comparison with others (Table 1). In addition, with increased bacilli density in the primary sputum sample, the time to sputum conversion after treatment was longer (Table 2). With increased age, the time it took for sputum to become negative was longer, but this relationship was not significant based on Spearman correlation coefficient ($r=0.15$, $P=0.17$).

Discussion

In this study, the mean time of sputum conversion in smear-positive pulmonary

tuberculosis patients was about 2 months. In addition, it was revealed that the time that sputum became negative was longer in males and in those with pre-existing chronic disease. With increased bacilli density prior to treatment initiation, the time to sputum conversion was longer. These findings are comparable to a study from Portugal that was carried out in 2012.⁴ Furthermore, 64.7% of patients showed smear conversion until the end of the second month and this figure reached 91.8% at the end of the third month. At the end of the fourth month, 98.8% showed smear conversion. In a study performed by Soudbakhsh² in 2001, 74.6% of patients had negative smears at the end of the second month of treatment and until the end of the third and fourth months, 83.9% and 85.3% had negative smears, respectively.

Sputum smear negativity is a sign that indicates response to anti-tuberculosis treatment. Sputum with a specificity of 95% is a diagnostic test to evaluate treatment response. Therefore, sputum negativity is the best marker to evaluate treatment response. Tahir et al, demonstrated that tuberculosis organism smear and culture have a significant relationship, but culture is time consuming and may not show the organisms in case of low sputum volume. Consequently, culture is not appropriate to follow all patients.³

The rate of smear negativity at the end of the second month (64.7%) was in agreement with a study done in Oman, but different from studies in Bangladesh (85% response) and India (91% response).⁶

In this study, it was revealed that with increased initial sample bacilli density, the time to smear negativity was prolonged. This is compatible with studies performed by Soudbakhsh² and Gopi.⁷ In addition, patients whose pulmonary involvement was evident on two or more views, the time to smear negativity was longer, which is consistent with studies by Soudbakhsh² and Guler.⁵

Unsematham et al. noted that the presence of cavity in pulmonary tuberculosis patients is associated with delayed smear negativity.⁸ Although some of our patients had cavity in their lungs, but no significant relationship was found between the presence of cavity and smear conversion. This is in agreement with a study in Oman.⁹

In patients with high load of bacilli, tissue destruction is more prominent, which is due to a weak immune system to control the disease. Furthermore, antibiotics have limitations in accessing organisms.^{7,10}

In our study, those with pre-existing disease (diabetes, chronic obstructive pulmonary disease (COPD), and chronic cardiac diseases) showed

Table 1: Comparison of mean sputum conversion time after treatment initiation in the studied patients

Variable	Statistical index	Frequency	Mean±SD (month)	Mann-Whitney test
Gender	Male	38	2.29±1.23	P=0.046*
	Female	47	1.74±0.85	
Pre-existing medical illness	Yes	38	2.42±1.13	P=0.001*
	No	47	1.64±0.87	
Residence place	Urban	47	2±1.08	P=0.92
	Rural	38	1.97±1.05	
The number of radiographic views	1 view	36	1.75±0.94	P=0.09
	≥2 views	49	2.16±1.12	
COPD	Yes	5	3±1.22	P=0.04
	No	80	1.92±1.03	
Bilateral pulmonary involvement	Yes	23	2.39±1.2	P=0.052
	No	62	1.84±0.98	
Smoking habits	Yes	14	2.5±1.45	P=0.14
	No	71	1.89±0.95	

COPD: Chronic obstructive pulmonary diseases, SD: Standard deviation, *Significance at alpha=0.05

Table 2: Comparison of sputum conversion after starting treatment in the studied patients based on the primary bacilli density

Primary bacilli density	Frequency	Mean±SD (month)	P value obtained from Kruskal-Wallis and Mann-Whitney tests
1+	25	1.32±0.56	P<0.001; Kruskal-Wallis test*
2+	21	1.71±0.85	P<0.001: 1+ and 3+
3+	39	2.56±1.12	P=0.004: 2+ and 3+

*Significance at alpha=0.05

delay in smear negativity compared with those without pre-existing medical illness. According to similar studies, different results have been reported regarding the relationship between time to sputum conversion and diabetes and COPD.¹¹⁻¹³

In an Indian study, although patients with diabetes showed more conversion in comparison with non-diabetic patients, however, such relationship was not reported by the study in Oman. Supervision and control of diabetes can decrease the difference between well-controlled diabetes and non-diabetic patients.⁹

In our study, the time to sputum smear conversion was significantly longer in males compared with females. This is not compatible with results reported in other studies.¹³ However, in a study by Balasubrasekaran et al,¹⁴ it was reported that males experience more treatment failures. This could be due to irregular drug intake by men compared with women.

Although in older patients the time to smear conversion was prolonged, the relationship was not significant. In a study by Al-Mamari in Canada as well as a study from Oman, no significant relationship was detected between age and sputum negativity.³ However, a study by Arora et al. from India, showed that older patients had less sputum conversion compared with the youth.¹⁵ Pre-existing illnesses in older

patients and non-compliance in this age group could explain the cause of lower response rate.

The main limitations of the present study were the small sample size (limiting our ability to detect significant associations) and potential inaccuracies in completing the records (leading to bias in data collection). To minimize inaccuracies, the authors carefully reviewed all clinical files and available examination results.

Conclusion

In this study, it was revealed that pre-existing illness, smoking, bacilli density in initial smear, and severe involvement of the lung on radiography could be associated with delay in sputum smear conversion. It is recommended that (i) In future, such study should be done using sputum culture, (ii) Pre-existing illnesses of tuberculosis patients should be treated or controlled, (iii) DOTS should be done with more accuracy, specifically in patients with addiction, males, and those with pre-existing illnesses, and finally (iv) More studies with larger sample size in "at risk groups" should be carried out.

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Conflict of interest: None declared.

References

- Kayigamba FR, Bakker MI, Mugisha V, Gasana M, Schim van der Loeff MF. Sputum completion and conversion rates after intensive phase of tuberculosis treatment: an assessment of the Rwandan control program. *BMC Res Notes*. 2012;5:357. doi: 10.1186/1756-0500-5-357. PubMed PMID: 22800438; PubMed Central PMCID: PMC3413528.
- Soubhakhsh AR, Ahmadinejad Z, Sistanizadeh M. Sputum Conversion Among Patients With Smear Positive Pulmonary Tuberculosis. *Tehran Univ Med J*. 2003;61:47-56. Persian.
- Parikh R, Nataraj G, Kanade S, Khatri V, Mehta P. Time to sputum conversion in smear positive pulmonary TB patients on category I DOTS and factors delaying it. *J Assoc Physicians India*. 2012;60:22-6. PubMed PMID: 23405517.
- Caetano Mota P, Carvalho A, Valente I, Braga R, Duarte R. Predictors of delayed sputum smear and culture conversion among a Portuguese population with pulmonary tuberculosis. *RevPortPneumol*. 2012;18:72-9. doi: 10.1016/j.rppneu.2011.12.005. PubMed PMID: 22277838.
- Guler M, Unsal E, Dursun B, Aydin O, Capan N. Factors influencing sputum smear and culture conversion time among patients with new case pulmonary tuberculosis. *Int J Clin Pract*. 2007;61:231-5. doi: 10.1111/j.1742-1241.2006.01131.x. PubMed PMID: 17166185.
- Tahir M, Sharma SK, Rohrberg DS, Gupta D, Singh UB, Sinha PK. DOTS at a tertiary care center in northern India: successes, challenges and the next steps in tuberculosis control. *Indian J Med Res*. 2006;123:702-6. PubMed PMID: 16873915.
- Gopi PG, Chandrasekaran V, Subramani R, Santha T, Thomas A, Selvakumar N, et al. Association of conversion & cure with initial smear grading among new smear positive pulmonary tuberculosis patients treated with Category I regimen. *Indian J Med Res*. 2006;123:807-14. PubMed PMID: 16885603.
- Unsematham S, Kateruttanakul P. Factors predicting sputum smear conversion and treatment outcomes in new smear-positive pulmonary tuberculosis. *J Med Assoc Thai*. 2013;96:644-9. PubMed PMID: 23951819.
- Singla R, Khan N, Al-Sharif N, Ai-Sayegh MO, Shaikh MA, Osman MM. Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. *Int J Tuberc Lung Dis*. 2006;10:74-9. PubMed PMID: 16466041.
- Parikh R, Nataraj G, Kanade S, Khatri V, Mehta P. Time to sputum conversion in smear positive pulmonary TB patients on category I DOTS and factors delaying it. *J Assoc Physicians India*. 2012;60:22-6. PubMed PMID: 23405517.
- Viswanathan V, Vigneswari A, Selvan K, Satyavani K, Rajeswari R, Kapur A. Effect of diabetes on treatment outcome of smear-positive pulmonary tuberculosis--a report from South India. *J Diabetes Complications*. 2014;28:162-5. doi: 10.1016/j.jdiacomp.2013.12.003. PubMed PMID: 24461545.
- Lonroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Soc Sci Med*. 2009;68:2240-6. doi: 10.1016/j.socscimed.2009.03.041. PubMed PMID: 19394122.
- Dembele SM, Ouedraogo HZ, Combarry A, Saleri N, Macq J, Dujardin B. Conversion rate at two-month follow-up of smear-positive tuberculosis patients in Burkina Faso. *Int J Tuberc Lung Dis*. 2007;11:1339-44. PubMed PMID: 18034956.
- Balasubramanian R, Garg R, Santha T, Gopi PG, Subramani R, Chandrasekaran V, et al. Gender disparities in tuberculosis: report from a rural DOTS programme in south India. *Int J Tuberc Lung Dis*. 2004;8:323-32. PubMed PMID: 15139471.
- Arora VK, Singla N, Sarin R. Profile of geriatric patients under DOTS in Revised National Tuberculosis Control Programme. *Indian J Chest Dis Allied Sci*. 2003;45:231-5. PubMed PMID: 12962456.