

Factors influencing delay in sputum smear conversion among new smear-positive pulmonary tuberculosis patients of Davangere tuberculosis unit

Anandaraj R¹, Anurupa M S², Kavithai P³, Rashmi B M⁴, Ranjitha A², Raghavendra S K⁵

¹Department of Community Medicine, Indira Gandhi Medical College and Research Institute, Puducherry, India, ²Department of Community Medicine, J.J.J. Medical College, Davangere, Karnataka, India, ³Department of Health and Family Welfare, Government of Puducherry, Puducherry, India, ⁴Department of Community Medicine, Basaveshwara Medical College and Hospital, Chithradurga, Karnataka, India, ⁵Department of Community Medicine, Adichunchanagiri Institute of Medical Sciences, Bellur, Karnataka, India

Correspondence to: Anandaraj R, E-mail: anand2469@gmail.com

Received: August 19, 2017; Accepted: September 13, 2017

ABSTRACT

Background: Sputum smear conversion rate (SCR) at the intensive phase (IP) of antitubercular treatment is an indicator of patient's response to treatment as well as the performance of tuberculosis (TB) control program, especially in resource-limited settings. **Objectives:** The objectives of this study are (1) to identify medicosocial factors associated with a delay in sputum smear conversion at the end of IP and (2) to find the influence of sputum smear conversion on treatment outcome. **Materials and Methods:** A prospective study was conducted in all six Designated Microscopy Centers (DMCs) of Davangere TB Unit, Karnataka, for 1 year. About 216 new sputum smear-positive pulmonary TB patients aged ≥ 15 years who were diagnosed in these DMCs and registered under Revised National TB Control Program constituted the study sample. Data were collected by direct interview method using a pretested, semistructured questionnaire. **Results:** Majority of the study subjects were males, residing in urban areas. The overall sputum SCR was 85.8%. Univariate analysis revealed that elderly age, stigmatization, tobacco smoking, diabetes mellitus, and pretreatment sputum smear grading were significantly associated with delayed sputum smear conversion at the end of IP. In multivariate analysis, tobacco smoking (adjusted odds ratio [aOR] [95% confidence interval (CI)]: 2.18 [1.03-4.61]), diabetes mellitus (aOR [95% CI]: 3.43 [1.27-9.31]), and higher pretreatment smear grading of 3⁺ (aOR [95% CI]: 2.73 [1.27-5.85]) emerged as independent predictors of delayed sputum smear conversion. Delayed sputum smear conversion was also found to be significantly linked with unfavorable treatment outcomes. **Conclusion:** Sputum SCR among new smear-positive pulmonary TB patients in Davangere TB Unit was satisfactory. Patients with identified risk factors were less likely to achieve sputum smear conversion and need to be monitored more closely to prevent unfavorable outcomes.


KEYWORDS: Designated Microscopy Center; New Smear Positive; Pulmonary Tuberculosis; Sputum Smear Conversion; Smear Conversion Rate; Sputum Smear Grading

INTRODUCTION

Tuberculosis (TB) is a major public health problem even after 20 years of its declaration as a global public health

emergency by the WHO.^[1] Started as pilot project in 1993 by Government of India, Revised National TB Control Program (RNTCP) scaled up nationwide by 2006.^[2] RNTCP recommends periodic sputum smear microscopy during the course of treatment to monitor patient progress and to assess overall program performance.^[2]

Change in the bacteriological status of sputum from initial acid-fast bacilli (AFB) positive to AFB negative after intensive phase (IP) of treatment is known as sputum smear conversion.^[2] Smear conversion rate (SCR) is a significant operational indicator as it shows the capacity of the program

Access this article online	
Website: http://www.ijmsph.com	Quick Response code
DOI: 10.5455/ijmsph.2017.0824913092017	

International Journal of Medical Science and Public Health Online 2017. © 2017 Anandaraj R, et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

to maintain patients on treatment. It also provides an objective evidence for the patient's response to therapy and hence the treatment outcome.^[2] Failure of sputum smear conversion has been considered as a predictor of patient infectivity and treatment failure or relapse.^[4]

Patients with positive smears after 2 months of treatment may not react well to treatment due to infection with drug-resistant *Mycobacterium* TB, one of the major risk factors for non-cure, and remain infectious for prolonged periods of time. It was observed in Bangladesh that non converters after 2 months of treatment were 40 times at risk of developing multidrug-resistant TB (MDR-TB).^[5] In the era of drug-resistant TB, the nation has only 64 RNTCP certified laboratories capable of performing culture and drug sensitivity testing (CDST).^[6] This works out to a very low ratio of 0.05 CDST laboratories per million population. Although RNTCP is slowly scaling up the CDST laboratory network, not all are able to get screened for drug resistance.

In such a scenario, identification of factors associated with persistent sputum positivity at the end of IP may be helpful in stratifying such patients. This stratification may improve TB control activities in the context of drug resistance by prioritizing those patients for screening for drug resistance.

Keeping in mind the above facts, the present study was conducted among new smear-positive pulmonary TB patients to identify medicosocial factors associated with a delay in sputum smear conversion at the end of IP and also the influence of smear conversion on treatment outcome.

MATERIALS AND METHODS

Davangere TB unit is located in the central part of Karnataka state in south India. It covers a population of over 600,000^[7] and has six Designated Microscopy Centers (DMCs) functioning under RNTCP for the diagnosis of TB. This prospective study was carried out in these six DMCs of Davangere TB unit. All new sputum smear-positive pulmonary TB patients aged ≥ 15 years of either sex, registering for directly observed treatment, short course (DOTS) IP under RNTCP from 1st January 2014 to 31st December 2014 were enrolled. The study subjects were selected consecutively as and when they were registering during the study period. Previously treated TB patients, new smear-negative pulmonary TB, or extrapulmonary TB patients were excluded from the study.

Ethical approval was obtained from the Institutional Ethical Review Board. After obtaining informed consent, a pre-tested questionnaire was administered by "direct-interview" method to collect data regarding sociodemographic factors, clinical history, addictions, sputum smear grading, and comorbid conditions such as HIV, diabetes mellitus, and undernutrition. The pretreatment sputum smears were graded as scanty, 1⁺, 2⁺, or 3⁺. Patients were subjected to follow-up sputum

smears at the end of IP for smear conversion and at the end of continuation phase for the outcome as per the RNTCP guidelines.^[3]

Those patients who had obtained negative sputum smear status at the end of IP were considered as smear converters. Those patients who remained smear positive at the end of IP were considered as nonconverters. Favorable outcome was assigned for those who were either declared as cured or treatment completed. The remaining patients were considered to have an unfavorable outcome.

Adherence to DOTS was considered to be present if the patient had consumed $\geq 80\%$ of the prescribed drugs in the IP. To assess stigmatization, questions asked to include support of family members, abandoned by any, lost respect within family or community, and isolation within household. Enacted social stigma was arbitrarily considered to be present if it was evident in three or more of the abovementioned questions. Undernutrition was considered if the calculated body mass index was below 18.5 kg/m².^[8]

The collected data were compiled in Microsoft Excel worksheet and analyzed using Statistical Package for Social Sciences software version 18.0. Categorical variables were summarized using percentages and proportions. Chi-square test was employed for analyzing categorical data. Fisher's exact test was used when the expected value of more than 25% of the cells was < 5 . A *P* value below 0.05 was considered statistically significant. Logistic regression analysis was performed to find the predictors for the delay in sputum smear conversion.

RESULTS

Baseline Characteristics and Smear Conversion

A total of 233 patients registered for DOTS during the study period. Mean age of the study subjects was 41.9 ± 15.12 years. About 164 (70.4%) of them were men. Most were residents of the urban area (60.9%). Out of 233 patients, 5 (2.2%) patients died, 11 (4.7%) patients defaulted from treatment, and 1 (0.4%) was transferred out. Of the 216 patients available for the follow-up smear at the end of IP, 175 (75.1%) converted to smear negative at the end of IP, whereas 41 (17.6%) remained smear positive. These 41 patients were treated with extended IP phase, and among them, 25 (85.8%) got converted to smear negative and 16 (6.9%) still remained persistently smear positive at the end 3 months.

Factors Influencing Smear Conversion

After excluding 17 dropouts, factors influencing delay in sputum smear conversion at the end of IP of 216 study subjects were analyzed. Of the sociodemographic variables,

the age was found to have a significant association ($P = 0.03$) with delayed sputum smear conversion with crude odds ratio (OR) (95% confidence interval [CI]) of 2.15 (1.03-4.47). Study subjects older than 50 years were more likely to go for delayed conversion than subjects younger than 50 years. It was also observed that 29.3% in the delayed converters group were stigmatized as compared to only 15.4% of the converters group ($P = 0.03$). Smokers more often were found to have delayed conversion as compared to nonsmokers (65.9% vs. 34.1%, $P = 0.02$). These are depicted in Table 1. Among the comorbid conditions, diabetes mellitus was found to be significantly associated ($P = 0.01$) with delayed sputum smear conversion. HIV infection was not significantly associated ($P = 0.30$) with delayed smear conversion. An initial higher sputum smear grading of 3⁺ was found to be associated ($P = 0.03$) with delayed smear conversion when compared to lower smear grading such as 2⁺, 1⁺, and scanty (Table 2).

For multivariate analysis, all the variables with $P < 0.05$ in univariate analysis were entered as independent variables, and sputum smear conversion was entered as dependent variable. Higher pretreatment sputum smear grading (3⁺), presence of diabetes mellitus, and smoking were found to have significant adjusted OR and emerged as independent predictors of delayed sputum smear conversion at the end of IP (Table 3).

Sputum Smear Conversion and Treatment Outcome

Of the 216 study subjects, the outcome of 176 (81.5%) was favorable in terms of cured or treatment completed, whereas 40 (18.5%) had an unfavorable outcome such as default, failure, or death. Significantly more nonconverters, both at the end of IP (37.5% vs. 14.8%) and at the extended IP (32.5% vs. 1.7%), were having unfavorable outcomes as compared to converters. Delay in sputum smear conversion

Table 1: Association of sociodemographic and clinical factors with smear conversion ($n=216$)

Variable	Converted	Not converted	P value	Unadjusted OR (95% CI)
Age (years)				
<50	138 (78.9)	26 (63.4)	0.03	2.15 (1.03-4.47)
≥50	37 (21.1)	15 (36.6)		
Gender				
Male	120 (68.6)	30 (73.2)	0.56	0.80 (0.37-1.71)
Female	55 (31.4)	11 (26.8)		
Domicile				
Rural	73 (41.7)	12 (29.3)	0.14	1.73 (0.82-3.61)
Urban	102 (58.3)	29 (70.7)		
Education				
Illiterate	93 (53.1)	21 (51.2)	0.82	1.08 (0.54-2.13)
Literate	82 (46.9)	20 (48.8)		
Social stigma				
Absent	148 (84.6)	29 (70.7)	0.03	2.26 (1.03-4.98)
Present	27 (15.4)	12 (29.3)		
Adherence				
Present	157 (89.7)	36 (87.8)	0.94	1.21 (0.42-3.47)
Absent	18 (10.3)	5 (12.2)		
Side effects ATT				
Absent	97 (55.4)	18 (43.9)	0.18	1.58 (0.80-3.15)
Present	78 (44.6)	23 (56.1)		
Family H/O TB				
Absent	148 (84.6)	32 (78.0)	0.31	1.54 (0.66-3.59)
Present	27 (15.4)	9 (22.0)		
Alcohol				
No	92 (52.6)	20 (48.8)	0.66	1.16 (0.58-2.29)
Yes	83 (47.4)	21 (51.2)		
Smoking tobacco				
No	94 (53.7)	14 (34.1)	0.02	2.23 (1.10-4.55)
Yes	81 (46.3)	27 (65.9)		

TB: Tuberculosis, ATT: Antituberculosis therapy, OR: Odds ratio, CI: Confidence interval

Table 2: Association of comorbid conditions and initial smear grading with smear conversion ($n=216$)

Variable	Converted	Not converted	P value	Unadjusted OR (95% CI)
HIV				
Absent	160 (91.4)	40 (97.6)	0.31	0.26 (0.03-2.07)
Present	15 (8.6)	1 (2.4)		
Diabetes mellitus				
Absent	157 (89.7)	31 (75.6)	0.01	2.81 (1.18-6.67)
Present	18 (10.3)	10 (24.4)		
Undernutrition				
Absent	25 (14.3)	10 (24.4)	0.11	0.51 (0.22-1.18)
Present	150 (85.7)	31 (75.6)		
Initial smear grading				
2 ⁺ , 1 ⁺ , scanty	117 (66.9)	20 (48.8)	0.03	2.11 (1.06-4.21)
Grade 3 ⁺	58 (33.1)	21 (51.2)		

OR: Odds ratio, CI: Confidence interval

Table 3: Predictors of smear conversion by multivariate analysis ($n=216$)

Variable	P value	Adjusted OR	95% CI
Age ≥ 50 years	0.27	1.57	0.69-3.55
Stigmatization	0.08	2.14	0.91-5.03
Smoking tobacco	0.04	2.18	1.03-4.61
Diabetes mellitus	0.01	3.43	1.27-9.31
Initial smear grading 3 ⁺	0.01	2.73	1.27-5.85

OR: Odds ratio, CI: Confidence interval

was found to be significantly associated with unfavorable treatment outcomes (Table 4).

DISCUSSION

As per the RNTCP, SCR of at least 85-90% has to be achieved in a well-performing area.^[2] The cumulative SCR in the present study was 85.8% which was slightly lower than the state (88%) as well as national (90%) rates.^[9] Higher SCRs of more than 85% has been noted in other parts of the country.^[10-17]

Mota *et al.*^[18] in Portugal observed that age above 50 years was significantly associated ($P = 0.008$) with delayed smear conversion. A similar result was observed by other authors as well.^[4,19-22] Reason for elderly patients having higher rates of nonconversion may be due to possible age-related immune dysregulation and delay in seeking health care which might lead to progression of the disease.^[23,24]

In our study, although men had higher rates of delayed conversion at 2 months than females (73.2% vs. 26.8%), gender was not significantly associated with delayed smear conversion. This may be due to a higher proportion of males in our study. However, studies done elsewhere have observed a significant association of gender with smear conversion.^[18,25]

Many studies have documented demographic, medical, microbiological, and radiological factors influencing sputum smear conversion,^[4,13,19,25-27] but none of them have focused on social factors. TB being a well-known example of stigmatizing disease, we made an attempt to look into the effect of stigmatization on smear conversion. The possible influence of social stigma on smear conversion can be explained by the loss of support, both economical as well as emotional, coupled with neglect by family and community. The interplay of these multiple social factors may lead to lowered adherence to anti-TB therapy (ATT), and also nutrition deprivation due to neglect which in turn may result in a delay in smear conversion, as evident in our results.

Although the proportion of subjects not adherent to antitubercular drugs was more in delayed converters than converters, a significant association could not be established. This could be due to the absence of standard criteria under the national program to define adherence in ATT.

Smoking as an independent predictor of smear conversion has been proven by other studies as well.^[22,28,29] Tobacco smoke inhibits the defense mechanism of lung against infections.^[30] It stimulates the alveolar macrophages for an inflammatory response and also suppresses the antigen presentation function to develop a specific immune response, thereby causing T cell anergy.^[30-33] Thus, there exists an immunodeficiency pattern in smokers which leads to the delayed clearing of bacilli from their lungs.

Diabetics were thrice more prone to have a delayed smear conversion in our study. Studies conducted elsewhere also reiterate this fact.^[34-37] Defects in the immune system of patients with active TB and diabetes lead to reductions in the activation of alveolar macrophages^[38] and the capacity to produce interleukins,^[39] resulting in delayed smear conversion.

Table 4: Association of smear conversion with treatment outcome ($n=216$)

Conversion	n (%)		P value	OR (95% CI)
	Favorable outcome	Unfavorable outcome		
At end of 2 months	150 (85.2)	25 (62.5)	0.00	3.46 (1.61-7.42)
Converted	26 (14.8)	15 (37.5)		
Not converted				
At end of 3 months	173 (98.3)	27 (67.5)	0.00	27.76 (7.42-103.86)
Converted	3 (1.7)	13 (32.5)		
Not converted				

OR: Odds ratio, CI: Confidence interval

We observed that HIV-infected study subjects were more prone for going to early conversion than delayed conversion (8.6% vs. 2.4%, $P = 0.30$). Domínguez-Castellano *et al.*^[40] observed that the period of conversion was significantly shorter in HIV patients (median: 18 days) than those not infected with HIV (median: 30 days). As HIV infection progresses and CD4 cells are depleted, the host immune response becomes less effective. Hence, cavity formation and sputum smear positivity are less common in HIV-infected TB patients.^[3,40-42] Although the study conducted elsewhere showed a significant influence of undernutrition on smear conversion,^[43] the present study could not. This may be attributed to geographical differences.

Influence of pretreatment bacillary load on sputum smear conversion in TB patients has been extensively researched in the past.^[4,18,19,21,44,45] Patients with higher initial smear grading reflect the higher bacillary load in their lungs, with a corresponding increase in cavity formation.^[46]

Earlier studies showed significantly lower cure rates and higher failure rates for those failing to achieve smear conversion at the end of IP.^[44,47,48] The present study supports this fact, thereby emphasizing the important relation between smear conversion and treatment outcome.

Self-reported status of diabetes and non-utilization of standardized tools for measuring social stigma are some of the limitations of our study.

CONCLUSION

The SCR among previously untreated TB patients in the study area appears to be satisfactory. Smear conversion was unlikely in patients with certain risk factors, thereby leading to poor outcomes. We would like to recommend for prioritization of TB patients with tobacco smoking, diabetes mellitus, or higher initial smear grading (3⁺) for initial screening for drug resistance, as these patients are at higher risk of nonconversion. Orientation about the importance of regular follow-up sputum examinations needs to be emphasized to TB patients, to foresee drug resistance in them as well as to reduce the risk of transmission to the community. Literacy

and empowerment would pave a long way to address the deeply rooted social stigma regarding this disease.

REFERENCES

1. World Health Organization. TB: A Global Emergency. WHO Report on TB Epidemic? Geneva: World Health Organization; 1994.
2. Government of India. Revised National Tuberculosis Control Programme. Training Course for Program Manager (Modules 1-4). Central TB Division. Directorate General of Health Services. New Delhi: Ministry of Health and Family Welfare; 2011.
3. Toman K. Toman's Tuberculosis. Case Detection, Treatment, and Monitoring: Questions and Answers. 2nd ed. Geneva: World Health Organization; 2004.
4. Singla R, Osman MM, Khan N, Al-Sharif N, Al-Sayegh MO, Shaikh MA. Factors predicting persistent sputum smear positivity among pulmonary tuberculosis patients 2 months after treatment. *Int J Tuberc Lung Dis*. 2003;7(1):58-64.
5. Flora MS, Amin MN, Karim MR, Afroz S, Islam S, Alam A, *et al.* Risk factors of multi-drug-resistant tuberculosis in Bangladeshi population: A case control study. *Bangladesh Med Res Counc Bull*. 2013;39(1):34-41.
6. Government of India. TB India 2015. RNTCP Status Report. Central TB Division. Directorate General of Health Services. New Delhi: Ministry of Health and Family Welfare; 2015.
7. Registrar General of India. Census of India. Provisional Population Totals-Karnataka Data Sheet. Office of the Registrar General Census Commissioner. India: Indian Census Bureau; 2011.
8. WHO. Physical Status: The Use and Interpretation of Anthropometry. Report of a WHO Expert Consultation. WHO Technical Report Series Number 854. Geneva: World Health Organization; 1995.
9. Government of India. TB India. RNTCP Status Report. Central TB Division. Directorate General of Health Services. New Delhi: Ministry of Health and Family Welfare; 2014.
10. Vasudevan K, Jayakumar N, Gnanasekaran D. Smear conversion, treatment outcomes and the time of default in registered tuberculosis patients on RNTCP DOTS in Pondicherry, Southern India. *J Clin Diagn Res*. 2014;8(10):JC05-8.
11. Bawri S, Ali S, Phukan C, Tayal B, Barua P. A study of sputum conversion in new smear positive pulmonary tuberculosis cases at the monthly intervals of 1st, 2nd and 3rd month under directly observed treatment, short course (DOTS) regimen. *Lung India*.

- 2008;25:118-23.
12. Srinivas K, Shreedevi A. A study on treatment outcome of new sputum smear positive tuberculosis patients among tribal population in Kurnool district. *Int J Res Dev Health.* 2013;1(1):5-10.
 13. 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.
 14. Joseph N, Nagaraj K, Bhat J, Babu R, Kotian S, Ranganatha Y, et al. Treatment outcomes among new smear positive and in M retreatment cases of tuberculosis angalore, South India - A descriptive study. *Australas Med J.* 2011;4(4):162-7.
 15. Mukherjee A, Singla R, Saha I, Sarkart A, Bhattacharyya P. Difference in the outcome of patients with different grades of initial sputum positivity under the revised National Tuberculosis Control Programme. *Indian J Chest Dis Allied Sci.* 2011;53(4):241-2.
 16. Kaur G, Goel NK, Kumar D, Janmeja AK, Swami HM, Kalia M. Treatment outcomes of patients placed on treatment under directly observed therapy short-course (DOTS). *Lung India.* 2008;25(2):75-7.
 17. Chadha SL, Bhagi RP. Treatment outcome in tuberculosis patients placed under directly observed treatment short course (DOTS) - A cohort study. *Ind J Tub.* 2000;47(3):155-58.
 18. Mota PC, Carvalho A, Valente I, Braga R, Duarte R. Predictors of delayed sputum smears and culture conversion among a Portuguese population with pulmonary tuberculosis. *Rev Port Pneumol.* 2012;18(2):72-9.
 19. Rekha VV, Balasubramanian R, Swaminathan S, Ramachandran R, Rahman F, Sundaram V, et al. Sputum conversion at the end of intensive phase of category-I regimen in the treatment of pulmonary tuberculosis patients with diabetes mellitus or HIV infection: An analysis of risk factors. *Indian J Med Res.* 2007;126(5):452-8.
 20. Djouma FN, Noubom M, Ateudjieu J, Donfack H. Delay in sputum smear conversion and outcomes of smear-positive tuberculosis patients: A retrospective cohort study in Bafoussam, Cameroon. *BMC Infect Dis.* 2015;15:139.
 21. Kigozi NG, Chikobvu P, Heunis JC, van der Merwe S. A retrospective analysis of two-month sputum smear non-conversion in new sputum smear positive tuberculosis patients in the free state province, South Africa. *J Public Health Afr.* 2014;5(324):68-72.
 22. Nagu TJ, Spiegelman D, Hertzmark E, Aboud S, Makani J, Matee MI, et al. Anemia at the initiation of tuberculosis therapy is associated with delayed sputum conversion among pulmonary tuberculosis patients in Dar-es-Salaam, Tanzania. *PLoS One.* 2014;9(3):e91229.
 23. Gaur SN, Dhingra VK, Rajpal S, Aggarwal JK, Meghna. Tuberculosis in the elderly and their treatment outcome under DOTS. *Indian J Tuberc.* 2004;51:83-7.
 24. Arora VK, Singla N, Sarin R. Profile of geriatric patients under DOTS in the revised national tuberculosis control programme. *Indian J Chest Dis Allied Sci.* 2003;45:231-5.
 25. Demebele 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(12):1339-44.
 26. Ukwaja KN, Oshi DC, Oshi SN, Alobu I. Profile and treatment outcome of smear-positive TB patients who failed to smear convert after 2 months of treatment in Nigeria. *Trans R Soc Trop Med Hyg.* 2014;108(7):431-8.
 27. Kayigamba FR, Bakker MI, Mugisha V, Gasana M, 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.
 28. Babalik A, Kiziltas S, Arda H, Oruc K, Cetintas G, Calisir HC. Factors affecting smear conversion in tuberculosis management. *Med Sci.* 2012;1(4):351-62.
 29. Maciel EL, Brioschi AP, Peres RL, Guidoni LM, Ribeiro FK, Hadad DJ, et al. Smoking and 2-month culture conversion during anti-tuberculosis treatment. *Int J Tuberc Lung Dis.* 2013;17(2):225-8.
 30. Gupta PC, Pednekar MS, Parkin DM, Sankaranarayanan R. Tobacco associated mortality in Mumbai (Bombay) India. Results of the Bombay cohort study. *Int J Epidemiol.* 2005;34(6):1395-402.
 31. Geng Y, Savage SM, Johnson LJ, Seagrave J, Sopori ML. Effects of nicotine on the immune response. I. Chronic exposure to nicotine impairs antigen receptor-mediated signal transduction in lymphocytes. *Toxicol Appl Pharmacol.* 1995;135(2):268-78.
 32. Wang JY, Hsueh PR, Jan IS, Lee LN, Liaw YS, Yang PC, et al. The effect of smoking on tuberculosis: Different patterns and poorer outcomes. *Int J Tuberc Lung Dis.* 2007;11(2):143-9.
 33. Geng Y, Savage SM, Razani-Boroujerdi S, Sopori ML. Effects of nicotine on the immune response. II. Chronic nicotine treatment induces T cell anergy. *J Immunol.* 1996;156(7):2384-90.
 34. Shariff NM, Safian N. Diabetes mellitus and its influence on sputum smear positivity at the 2nd month of treatment among pulmonary tuberculosis patients in Kuala Lumpur, Malaysia: A case control study. *Int J Mycobacteriol.* 2015;4(4):323-9.
 35. Mi F, Tan S, Liang L, Harries AD, Hinderaker SG, Lin Y, et al. Diabetes mellitus and tuberculosis: Pattern of tuberculosis, two-month smear conversion and treatment outcomes in Guangzhou, China. *Trop Med Int Health.* 2013;18(11):1379-85.
 36. Jiménez-Corona ME, Cruz-Hervert LP, García-García L, Ferreyra-Reyes L, Delgado-Sánchez G, Bobadilla-Del-Valle M, et al. Association of diabetes and tuberculosis: Impact on treatment and post-treatment outcomes. *Thorax.* 2013;68(3):214-20.
 37. Viswanathan AA, Gawde NC. Effect of Type II diabetes mellitus on treatment outcomes of tuberculosis. *Lung India.* 2014;31(3):244-8.
 38. Wang CH, Yu CT, Lin HC, Liu CY, Kuo HP. Hypodense alveolar macrophages in patients with diabetes mellitus and active pulmonary tuberculosis. *Tuber Lung Dis.* 1999;79(4):235-42.
 39. Yaghini N, Mahmoodi M, Asadikaram GR, Hassanshahi GH, Khoramdelazad H, Arababadi M. Serum levels of interleukin 10 (IL-10) in patients with Type 2 diabetes. *Iran Red Crescent Med J.* 2011;13(10):752.
 40. Dominguez-Castellano A, Muniain MA, Rodriguez-Bano J, Garcia M, Rios MJ, Galvez J, et al. Factors associated with time to sputum smear conversion in active pulmonary tuberculosis. *Int J Tuberc Lung Dis.* 2003;7:432-8.
 41. Telzak EE, Fazal BA, Pollard CL, Turett GS, Justman JE, Blum S. Factors influencing time to sputum conversion among patients with smear-positive pulmonary tuberculosis. *Clin Infect Dis.* 1997;25(3):666-70.
 42. Elliott AM, Hayes RJ, Halwiindi B, Luo N, Tembo G,

- Pobee JO, et al. The impact of HIV on infectiousness of pulmonary tuberculosis: A community study in Zambia. *AIDS*. 1993;7(7):981-7.
43. Putri FA, Burhan E, Nawas A, Soepandi PZ, Sutoyo DK, Agustin H, et al. Body mass index predictive of sputum culture conversion among MDR-TB patients in Indonesia. *Int J Tuberc Lung Dis*. 2014;18(5):564-70.
44. Tiwari S, Kumar A, Kapoor SK. Relationship between sputum smear grading and smear conversion rate and treatment outcome in the patients of pulmonary tuberculosis undergoing dots - A prospective cohort study. *Indian J Tuberc*. 2012;59(3):135-40.
45. Patel J, Dave P, Satyanarayana S, Kumar AM, Shah A, Ananthakrishnan R, et al. Pretreatment sputum smear grade and smear positivity during follow-up of TB patients in Ahmedabad, India. *Public Health Action*. 2013;3(4):308-10.
46. Jeremiah K, Praygod G, Faurholt-Jepsen D, Range N, Andersen AB, Grewal HM, et al. BCG vaccination status may predict sputum conversion in patients with pulmonary tuberculosis: A new consideration for an old vaccine? *Thorax*. 2010;65(12):1072-6.
47. Singla R, Bharty SK, Gupta UA, Khayyam KU, Vohra V, Singla N, et al. Sputum smear positivity at two months in previously untreated pulmonary tuberculosis patients. *Int J Mycobacteriol*. 2013;2(4):199-205.
48. Yellappa V, Kandpal V, Lall D, Tabassum A. Determinants of sputum conversion at two months of treatment under National Tuberculosis Programme, South India. *Int J Med Sci Public Health*. 2016;5:2416-20.

How to cite this article: Anandaraj R, Anurupa MS, Kavithai P, Rashmi BM, Ranjitha A, Raghavendra SK. Factors influencing delay in sputum smear conversion among new smear-positive pulmonary tuberculosis patients of Davangere tuberculosis unit. *Int J Med Sci Public Health* 2017;6(11):1565-1571.

Source of Support: Nil, **Conflict of Interest:** None declared.