Original Article

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Factors Influencing Sputum Smear Conversion among Smear Positive Pulmonary Tuberculosis Patients in Kandahar City, Afghanistan

Public Health Section

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ABSTRACT

Introduction: Sputum conversion is an important indicator of successful Tuberculosis (TB) treatment and control program. There is no published research on sputum conversion rate and its determinants, from Afghanistan.

Aim: To determine sputum smear conversion rate and identify the factors associated with delayed sputum conversion following TB treatment among smear positive pulmonary TB patients.

Materials and Methods: The study was based on a secondary data analysis of a retrospective cohort of 345 newly diagnosed sputum smear positive pulmonary TB patients, from 13 public health facilities in Kandahar city, Afghanistan during the year 2017. Data was extracted in a predesigned format, which included socio-demographic, clinical, microbiological, radiological, and treatment initiation and follow-up data from TB registers. Sputum conversion rate was presented as percentage. Bivariate analysis and multiple logistic regressions were used to identify the predictors of delayed sputum conversion.

Results: The mean age of the study participants was 38.3 years (SD±17.6). Of the total, 165 (48%) were male and 180 (52%) were female. About 83% study participants were successfully converted to sputum smear negative at the end of the intensive phase of treatment. On bivariate analysis, age group 50 years and above, female sex, haemoptysis at the first visit, and heavy bacterial load (sputum acid fast bacilli grading 3+) were found to be associated with delayed sputum conversion. Multiple logistic regression showed that heavy sputum bacterial load (adjusted odds ratio=15.7, 95% CI=7.82-31.6) was the single independent predictor of delayed conversion.

Conclusion: Higher sputum AFB grading has a greater risk of poor outcome than the patients with lower smear grading. Hence, the policy makers in Afghanistan should take a note of the results of this study to accelerate the TB control in the country.

Keywords: Bacterial load, *Mycobacterium tuberculosis*, TB control

INTRODUCTION

Tuberculosis (TB) is one of the oldest recorded human afflictions. It is a chronic infectious disease that can infect almost any part of the body predominantly affecting the lungs [1,2]. It is one of the major global health problems as it still ranks at top 10th cause of death. In the year 2016, an estimated 1.3 million people died from TB [3]. Low-income countries are severely affected by TB because of resources constraints and weak health systems to address the burden of TB [4]. Afghanistan ranked 21 among top 30 high TB burden countries until 2015 [3]. Afghanistan, with a population of 33 million, had 61000 cases in 2015. It is estimated that more than 25000 cases have been missed by the country's health system [5].

Sputum conversion rate is an important operational indicator of effectiveness of TB control program; and used to determine the duration in smear-positive patients to become smear negative under treatment [6]. In resource-intensive countries, it is recommended to document sputum culture conversion before completion of anti-TB treatment. However, sputum microscopy is simpler, faster and less expensive and hence, it is still recommended for diagnosis and assessment of treatment outcome in resources constraint countries [7].

Various studies have reported sputum conversion in smear-positive TB patients [3,8-11]. The proportion of TB patients who remain positive after two months of treatment can be greater than 20%. Sputum conversion rate in the studies conducted in Asia ranged from 73.4% to 78.6% in India, Iran and Pakistan. Gender, age, pre-existing medical illness, HIV infection, extensive cavitary lesion, high bacilli density, poor access to anti-TB treatment were found to be associated with delayed or poor sputum conversion [9-17]. More recently, resistance to anti-TB drugs is increasingly reported [6]. Evaluation of sputum conversion rate and understanding of the factors associated with delayed conversion is critical in reassuring treatment effectiveness as well as program effectiveness. Monitoring of the sputum conversion is important for treatment planning and assessing program effectiveness [8]. No study has been reported from Afghanistan on sputum conversion and TB patients.

Therefore, this study was aimed to assess sputum conversion rate and identify factors that cause delayed sputum conversion in newly diagnosed sputum positive pulmonary TB patients in Kandahar city, Afghanistan.

MATERIALS AND METHODS

Study Design and Population

This study was designed on retrospective cohort data analysis, using follow-up data of the patients from registration to treatment completion in the TB control program; from January to December 2016. Ethical approval of the study was obtained from the Institutional Committee for Ethics and Review of Research, IIHMR University, Jaipur (FWA#: FWA00018806, OMB No.0990-0279) and Kandahar Medical faculty research committee. Informed consent of patients was not sought, as we collected and analysed routine program data. Unique identifiers were removed from data analysis to ensure confidentiality of the study participants.

Study Setting

This study was conducted in 13 public health facilities and TB treatment centers in Kandahar city. These facilities provide services including testing, treating and counseling for TB to approximately 1 million urban populations. They are collaborative units of Ministry of Public Health and funded by international non-governmental organisations.

Study participants were newly diagnosed pulmonary TB cases, those who were registered at the selected public health facilities and TB treatment centres in Kandahar city. Newly diagnosed smear-positive pulmonary TB cases were defined according to WHO criteria [18].

Inclusion and exclusion criteria: Patients registered as category I TB (smear-positive) were included. Sputum negative, relapse, and drug resistant TB cases, or those died were excluded from the cohort.

Data Collection Methods

Data was collected during 2017-2018. The TB registers (National TB registers) of the health facilities were scrutinised starting from January to December 2016. Socio-demographic, clinical, microbiological, radiological, and treatment initiation and follow-up data were collected manually in the extracted sheet.

In the health facilities, suspected cases of TB were subjected to sputum microscopy. Pulmonary TB cases were classified according to bacteriological results. Sputum smear examination was done through microscopic observation of *M. tuberculosis* after staining with Ziehl-Neelsen's technique. The cases are classified as smear-negative pulmonary TB (smear contains no acid-fast bacilli (AFB) in 100 fields) and smear-positive pulmonary TB. Smear grading of the cases is done as follows: "1+ (10–99 AFB in 100 fields), 2+ (1–9 AFB/field in at least 50 fields), and 3+ (>10 AFB/field in at least 20 fields)" [18].

STATISTICAL ANALYSIS

Collected data were coded and entered into Microsoft Excel (2016). Data quality was checked for consistency, completeness, and accuracy.

The data were analysed using IBM SPSS version 21 [19]. Sputum conversion rates and delayed conversion were presented as percentages. Bivariate analysis was used for the possible factors associated with delayed sputum conversion. To determine the strength of association, Odds Ratio (Chi-square test, Mantel-Haenszel statistics) was estimated. Stepwise multiple logistic regressions (forward LR method) were carried out to identify independent predictors for delayed sputum conversion. The factors, which had an association with delayed sputum smear conversion on bivariate analysis, were included in the multiple regression analysis.

RESULTS

A total of 345 newly diagnosed smear-positive pulmonary TB patients who received category I treatment and had minimum five months follow-up data, were included in the analysis. The mean age of TB patients was 38 years (SD±17.6). Of the total, 52.2% were female, and 74% belonged to urban residence. All patients were HIV negative at initial visit. Major symptoms documented were fever (100%), cough (99%), chest pain (30%), night sweats (57.4%), weight loss (25%), and haemoptysis (24.3%). About 29% cases had primary bacilli density AFB1+, 43% AFB2+, and 27.8% AFB3+ before starting the treatment. [Table/Fig-1] shows socio-demographic factors, clinical, microbiological and other diagnostic findings at baseline.

The sputum conversion rate was 82.6% at the end of the 2nd month (intensive phase), and sputum smear conversion rate was delayed in 17.4% at the end of intensive phase of treatment.

Bivariate analysis of the factors associated with the delayed sputum conversion at two months of treatment is shown in [Table/Fig-2]. Patients who showed cavitary lesion and bilateral lesion on radiography had delayed sputum conversion, although it was not statistically significant. Age 50 years and above, female sex, haemoptysis at the first visit, and bacterial density of sputum AFB 3+ was significantly associated the delayed sputum conversion. These factors were included in the multiple logistic regression models. It was found that higher bacterial load (AFB3+) was significantly associated with delayed sputum conversion.

Characteristic		No of cases	Percentage
Age groups (Years)	1-14	23	6.7
	15-45	206	59.7
	46-60	63	18.3
	60 and above	53	15.4
Gender	Male	165	47.8
	Female	180	52.2
Type of residence	Urban	255	73.9
	Rural	90	26.1
Source of payment*	Government	345	100
Symptoms and signs	Fever	345	100
	Chest pain	103	29.9
	Cough	349	98.8
	Haemoptysis	84	24.3
	Weight loss	87	25.2
	Night sweats	198	57.4
Sputum microscopy	AFB1+	101	29.3
	AFB2+	148	42.9
	AFB3+	96	27.8
Chest X-ray (N=65; 18.8%)	Normal	8	2.3
	Abnormal	57	16.5
	- Cavitary lesion	3	0.9
	- Non-cavitary lesion	54	15.7
	OR		
	- Unilateral lesion	33	9.6
	- Bilateral lesion	24	7

[Table/Fig-1]: Baseline characteristics of enrolled patients (N = 345).
*All patients were recruited from public health facilities

Factor		*Unadjusted odds ratio (95% CI)	p-value	#Adjusted odds ratio (95% CI)	p-value
Sex	Male Female	1 1.89 (1.06-3.38)	0.030	1 0.8 (0.40-1.6)	0.550
Age	<50 years ≥50 years	1 1.97 (1.10-3.52)	0.022	1 0.6 (0.33-1.62)	0.225
Haemoptysis	Absent Present	1 2.28 (1.26-4.12)	0.006	1 1.7 (0.85-1.52)	0.127
AFB 3+ (initial visit)	No Yes	1 17.4 (8.76-34.61)	0.000	1 15.7 (7.81-31.6)	<0.0001

[Table/Fig-2]: Factors associated with delayed sputum smear conversion: unadjusted and adjusted odds ratio.
*Sputum smear conversion at the end of 2 months; #Odds ratio adjusted for sex, age, haemoptysis

DISCUSSION

This study was done to determine the sputum conversion rate at the intensive phase of anti-TB treatment and identify the factors associated with delayed sputum conversion. Monitoring of sputum smear conversion provides inputs for planning of treatment, diagnostic, and counseling services for TB patients and opportunity to address the emerging epidemic of Multi-drug Resistant Tuberculosis (MDR TB) [19]. It has special importance in countries like Afghanistan affected from high disease burden and conflict affected weak health systems.

In this study, the sputum conversion rate was 82.6% at the end of intensive phase of treatment in smear-positive pulmonary TB, which was remarkably similar in the studies conducted in Pakistan, India, West Africa, and Iran (80.5%-84%) [10,11,14,16]. It may be an overestimation of real figure in this study as this study population consisted of only newly diagnosed persons in affected area which is dominated by those aged below 50 years, and the absence of HIV positives in the study population. According to published studies, the poor conversion is associated with resistant and transferred cases, and HIV positive patients

[9-13,15,17]. Although the conversion rate, in this study, was higher than other study conducted in Portugal which was 74.6% [12]; it was lower than Taiwan (89.9%) [20], Gambia (90%) [21], and Cameroon (92.4%) [22]. Variation in sputum conversion rates in different studies may also be attributed to differences in geographic locations, baseline bacillary load, study methods, and other non-explored factors.

This study revealed the higher bacilli density (AFB3+) as a single independent predictor of delayed sputum conversion at the end of two months of treatment. Heavy bacterial load at initial testing was documented as an important risk factor of delay in sputum smear conversion at the end of intensive phase of TB treatment in the literature. Several studies have found high bacterial load as an important predictor of delayed conversion (Iran and Portugal – AFB2+ and AFB3+ [11,12], and Pakistan, Burkina Faso, and Rwanda – AFB3+ [10,13,14]). The patients with heavy bacterial load are at higher risk of delayed sputum conversion, development of MDR TB, and associated poor outcomes of treatment [11,23,24]. Hence, all TB patients should be identified and treated at the earliest to avoid delayed conversion. Further research is required to detect the determinants of heavy initial bacterial load among smear-positive pulmonary TB patients.

In addition to heavy bacterial load, an association between delayed sputum smear conversion and old age, female sex, and haemoptysis was also identified. Although, these factors did not achieve significance level in the multivariate analysis; it may be due to smaller sample size. Many studies in the past have reported that sputum conversion was higher in young patients [9-13,15,17]. Behnaz F et al., in Iran, and Caetano Mota P et al., in Portugal have also reported the association between the old age and the delayed conversion [11,12]. Poor conversion in old age might be due their increased incidence of physical disabilities, lack of efficacious bacilli clearance due to low immune response, and delay in seeking diagnosis and care. The co-morbidities associated with old age affecting anti-TB drug absorption and metabolism might be interfering with smear conversion in these patients [11].

In this study, TB was slightly preponderant among females (52.2%). This finding is similar to the WHO estimates (2016) for Afghanistan, where 63% of all newly diagnosed TB cases were women [5]. In contrast to this findings, studies in Iran, India, West Africa, and Portugal found that male sex was significantly associated with the delayed conversion [9,11,12,14]. The exact reason is not known but the severity of disease, illiteracy, and delayed presentation may play an important role. Cultural and financial barriers can act as major obstacles for women in seeking care, which results in delayed presentation and more severe illness especially in the conflict zones [5]. Women and children are the main victims of conflicts as their access to health care are limited [25].

Similar to these findings, a retrospective study conducted in Thailand have also reported that sputum smear conversion failure was associated with haemoptysis [26]. However, a study conducted in Cameroon found contradictory findings [27]. There is limited research which explored the association of symptoms with sputum conversion, thus more research and prospective studies are required to confirm these findings.

In this study, the patients with cavitary and bilateral lesion showed delayed conversion, but it was not statistically significant. Previous studies from India found that cavitary lesion and bilateral involvement was significantly associated with delayed conversion [9]. Small sample size and retrospective design of our study limit us on making conclusions on this finding in our study.

LIMITATION AND STRENGTH

This study was a secondary analysis of TB patients' treatment follow-up data. Therefore, it is difficult to comment on the causality of identified determinants. Being routine data of health services, this data set suffered from incompleteness, inaccuracy, and missing data such as chest radiograph findings, however, the authors carefully examined all registers to minimise these limitations. In addition, the potential risk factors not found in the registers were not assessed such as vitamin D deficiency, diabetes, nutritional status, etc. Although, this study has a small sample size which restricts its scope to generalise the findings; it is the first study of its kind from Afghanistan populations.

CONCLUSION

In this study, the delayed sputum conversion rate of newly diagnosed smear-positive pulmonary TB patients was 17.4% at the end of the intensive phase. The sputum microscopy finding AFB3+ was the single independent factor that could significantly predict sputum conversion. Hence, the policymakers in Afghanistan should take a note of the results of this study to accelerate the TB control in the country and the need of prospective studies to identify other risk factors associated with delayed conversion and unfavorable treatment outcomes.

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REFERENCES

[1] Smith I. *Mycobacterium tuberculosis* pathogenesis and molecular determinants of virulence. Clin Microbiol Rev. 2003;16(3):463-96. doi:10.1128/CMR.16.3.463-496.2003.
[2] Delogu G, Sali M, Fadda G. The biology of *Mycobacterium tuberculosis* infection. Mediterranean Journal of Hematology and Infectious Diseases. 2013;5(1):e2013070. doi:10.4084/MJHID.2013.070. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3867229/.
[3] World Health Organization. Global Tuberculosis Report; 2017. Geneva, 2017 Available from: http://www.who.int/tb/publications/global_report/en/.
[4] World Health Organization. Addressing poverty in TB control. Options for national TB control programmes. World Health Organization (2005).
[5] World Health Organization. Tuberculosis Profile, Afghanistan. 2015. Available from: http://www.who.int/tb/country/data/profiles/en/.
[6] Stop TB Partnership. Compendium of indicators for monitoring and evaluating National Tuberculosis Programs [Internet]. Geneva; 2004. Available from: https://www.challengetb.org/publications/tools/me/Compendium_of_Indicators_for_ME_NTPs.pdf.
[7] World Health Organization. Treatment of tuberculosis: guidelines- 4th ed. WHO/HTM/TB/2009.420. Geneva:WHO; 2010. Available from: http://www.who.int/tb/publications/2010/9789241547833/en/.
[8] Schwartzman K, Menzies D. How long are TB patients infectious? C Can Med Assoc J [Internet]. 2000;163(2):157-58. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC80198/.
[9] Sheetal D Vora, Rina V Gandhi SAV. A study of factors affecting sputum conversion in patients of pulmonary tuberculosis. Ntl J Community Med. 2016;7(2):01-05.
[10] D'Souza KA, Zaidi SMA, Jaswal M, Butt S, Khowaja S, Habib SS, et al. Factors associated with month 2 smear non-conversion among Category 1 tuberculosis patients in Karachi, Pakistan. J Infect Public Health. 2017;10-12. Available from: http://linkinghub.elsevier.com/retrieve/pii/S1876034117301521.
[11] Behnaz F, Mohammadzadeh M, Mohammadzade G. Five-Year assessment of time of sputums smears conversion and outcome and risk factors of tuberculosis patients in central Iran. Tuberc Res Treat. 2015;2015:609083.
[12] 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. Rev Port Pneumol. 2012;18(2):72-79. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22277838.
[13] Dembele SM, Ouedraogo HZ, Combary 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.
[14] 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(1):357. Available from: https://bmcresnotes.biomedcentral.com/articles/10.1186/1756-0500-5-357.
[15] Rajpal S, Dhingra VK, Aggarwal JK. Sputum grading as predictor of treatment outcome in pulmonary tuberculosis. Indian J Tuberc. 2002;49:139-42.

[16] Bawri S, Ali S, Phukan C, Tayal B, Baruwa P. A study of sputum conversion in new smear positive pulmonary tuberculosis cases at the monthly intervals of 1, 2 & 3 month under directly observed treatment, short course (dots) regimen. Lung India. 2008;25(3):118-23. doi: 10.4103/0970-2113.44122. Available from: http://dx.doi.org/10.4103/0970-2113.44122.
[17] Unsematham S KP. Factors predicting sputum smear conversion and treatment outcomes in new smear-positive pulmonary tuberculosis. J Med Assoc Thai. 2013;(96):6.
[18] World Health Organization. Definitions and reporting framework for tuberculosis-2013 revision. 2014 [cited 2017 Jun 29];09-11. Available from: http://apps.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf.
[19] IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.
[20] Chang LY, Lee CH, Chang CH, Lee MC, Lee MR, Wang JY, Lee LN. Acute biliary events during anti-tuberculosis treatment: Hospital case series and a nationwide cohort study. BMC Infect Dis. 2018;18:64. doi: 10.1186/s12879-018-2966-3.
[21] Lienhardt C, Manneh K, Bouchier V, Lahai G, Milligan PJ, McAdam KP. Factors determining the outcome of treatment of adult smear-positive tuberculosis cases in The Gambia. Int J Tuberc Lung Dis. 1998;2(9):712-18.
[22] 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(1):139. doi:10.1186/s12879-015-0876-1.
[23] Yihunie Akalu T, Muchie KF, Alemu Gelaye K. Time to sputum culture conversion and its determinants among Multi-drug resistant tuberculosis patients at public hospitals of the Amhara Regional State: A multicenter retrospective follow up study. Munderloh UG, ed. PLoS One. 2018;13(6):e0199320. doi:10.1371/journal.pone.0199320.
[24] Gunda DW, Nkandala I, Kavishe GA, Kilonzo SB, Kabangila R, Mpondo BC. Prevalence and risk factors of delayed sputum conversion among patients treated for smear positive PTB in northwestern rural Tanzania: A retrospective cohort study. J Trop Med. 2017;2017:5352906. doi:10.1155/2017/5352906.
[25] Khan IM, Laaser U. Burden of tuberculosis in Afghanistan: Update on a war-stricken country. Croat Med J. 2002;43:245-47.
[26] Rahimy N, Luvira V, Charunwatthana P, Iamsirithaworn S, Sutherat M, Phumratanaprapin W, et al. Predicting factors of treatment failure in smear positive pulmonary tuberculosis: a retrospective cohort study in Bangkok using a combination of symptoms and sputum smear/chest radiography. J Med Assoc Thai 2018;101:181-88.
[27] Pefura-Yone EW, Kengne AP, Kuaban C. Non-conversion of sputum culture among patients with smear-positive pulmonary tuberculosis in Cameroon: A prospective cohort study. BMC Infect Dis [Internet]. 2014;14:138. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3984706/.

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