



INITIAL SPUTUM SMEAR GRADING IS A PREDICTOR OF SMEAR CONVERSION AND TREATMENT OUTCOME IN PULMONARY TUBERCULOSIS: A RETROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Tuberculosis is an important public health problem. The Smear Conversion Rate (SCR) is an operational indicator for the Directly Observed Treatment Short course strategy of Revised National Tuberculosis Control Programme (RNTCP) in India. This study was conducted to determine the initial sputum smear grading and to assess the smear conversion rate (SCR) and treatment outcome.

Materials and Methods: This retrospective cohort study was conducted among 341 sputum smear positive patients from tuberculosis units of North 24 Parganas district. Record of initial smear grading, conversion and outcome of all new sputum smear positive patients were utilized. All patients were followed up periodically under the RNTCP guidelines.

Result: Total numbers of newly diagnosed smear positive TB patients collected were 341. Among them sputum grading were high positive cohort (3+) 24.6% and low positive cohort (scanty, 1+ and 2+) 75.4%. The conversion rates were observed for Scanty, 1+, 2+ and 3+ at 81.7%, 82.2%, 76.5% and 52.4% respectively at the end of the intensive phase of the treatment. It has been estimated that approximately 50% of mycobacterial load was reduced after intensive phase in high grading cohort whereas it was more than 75% reduction in low grading cohort.

Conclusion: The conversion rate of sputum smear was found dependent on initial sputum grading. The conversion rate was low in high grade cohort but increase in low grade cohort. The conversion rate was probably decreased on high mycobacterial load.

Key words: Outcome, smear grading, sputum conversion, tuberculosis

INTRODUCTION

Tuberculosis (TB) is an important public health problem worldwide.¹ It has been estimated that in the world, one patient is newly infected with TB in every second, nearly 1% of the world population is infected every year and overall, one third of the world population is infected with Mycobacterium

TB.² The World Health Organization (WHO) and India's Revised National Tuberculosis Control Programme (RNTCP) recommended periodic sputum smear microscopy during the course of TB treatment to monitor progress of individual patient and assess overall programme performance.³ The follow-up microscopy examinations are scheduled

at end of intensive phase (after 2 months of starting treatment) and between the 4th and 6th month of anti-TB treatment, i.e. in the middle of the 'continuation phase' (CP).⁴ The result of this (mid-CP) follow-up examination may have clinical implications; a patient found sputum smear-positive at the 5th month of treatment (or later) is considered as not responding to treatment ('treatment failure') and is evaluated for possible drug resistance. However, the utility of mid-CP follow-up in India has been questioned in a study from South India.⁵ This study could not influence policy on mid-CP follow-up, possibly because it was done in a small geographic area during the initial years of the RNTCP. The cumulative burden of this follow-up is substantial with more than 800,000 sputum smear-positive cases registered under the RNTCP each year.⁶

The World Health Organisation (WHO) declared TB as a "Global Emergency" in March 1993.⁷ According to an estimate by the WHO, between 1999 and the year 2020 nearly one billion more people will be newly infected, 200 million will get sick and 70 million will die from TB if control measures are not strengthened.⁸ The DOTS strategy for TB control represents one of the major public health strategies of the recent times which have resulted in an important therapeutic breakthrough, not only in our country, but also all over the world. It has been documented that eight out of ten patients under DOTS regimen are cured.⁹ Nation-wide DOTS covers 632 district and 1114 million people under RNTCP all over the country.⁸ Eighty five percent of Pulmonary TB patients among the all new TB cases in India are responsible for the spreading of infection. Therefore Pulmonary TB is epidemiologically important and become the topmost priority from public health point view.

Keeping this background in mind, the study was conducted to determine the initial sputum smear grading and to assess the smear conversion rate (SCR) and treatment outcome.

MATERIAL AND METHODS

The study was conducted at a tuberculosis unit of North 24 Parganas, West Bengal, India during September 2014 to August 2015. The nature of study was retrospective cohort study. The data were collected from registers of tuberculosis unit of North 24 Parganas through a schedule developed by authors ratified by public health specialists.

All sputum smear-positive TB cases were registered for treatment under the RNTCP during September 2014 to August 2015 in the tuberculosis units of North 24 Parganas district. All new sputum smear-positive TB cases were included and

their initial sputum grading, sputum smear conversion and outcome were collected from the records in the study. Seriously ill extra pulmonary category 1 cases, all sputum smear negative cases and patients lost to follow up were excluded. All eligible cases of sputum smear-positive TB registered during the study period were included in this study. Total number of newly diagnosed smear positive TB patients collected was 355 and this was the sample size. Among them two patients were declared failure, six patients were transferred out, three patients were not followed up and three patients died. Ultimately total 341 patients were included in this study as final size. Complete enumeration as sampling design was adopted in this study.

Study Variables were sputum smear microscopy was done at the end of IP, at the end of extended IP (wherever applicable), at two months of CP and at end of treatment. The sputum grading was done as scanty, 1+, 2+ and 3+. Scanty means 1 to 9 AFB in 100 oil immersion fields. 1+ means 10-99 AFB in 100 oil immersion fields. 2+ means 1 to 10 AFB per oil immersion field in at least 50 fields. 3+ is more than 10 AFB per oil immersion field in at least 20 fields. Outcome of treatment was recorded as cured, treatment completed, died, default, failure and transfer-out, as per the standard WHO definitions.¹⁰ High positive cohort and low positive cohort were denoted as 3+ and scanty to 2+ respectively.¹¹

Analysis was done on a total number of 341 patients having sputum smear positive. Tests for statistically significant findings were done at 95% confidence intervals with Chi square tests and P value of <0.05 were considered significant.

RESULTS

Total number of newly diagnosed smear positive TB patients was 355. Ultimately total 341 patients were included in this study considering the exclusion criteria.

Table 1: Distribution of TB patients according to age and sex:

Age (yrs)	Male (n=230)	Female (n=111)	Total(n=341)
1-9	0(0.00%)	1 (0.90%)	1 (0.29%)
10-19	20 (8.69%)	22 (19.82%)	42 (12.31%)
20-29	36 (15.65%)	39 (35.14%)	75 (22.00%)
30-39	45 (19.57%)	13 (11.71%)	58 (17.01%)
40-49	58 (25.22%)	16 (14.41%)	74 (21.70%)
50-59	37 (16.08%)	13 (11.71%)	50 (14.66%)
60-69	25 (10.87%)	5 (04.50%)	30 (8.80%)
≥ 70	9 (03.91%)	2 (01.80%)	11 (3.23%)

Figure in parenthesis indicate percentage

Table 2: Treatment outcome of high positive cohort vs. low positive cohort

Patients initiated on DOTS	Cured	Treatment Completed	Defaulted	Failure	Transferred out	Died
High positive cohort (n=195)	184 (94.36)	2 (01.03)	2 (01.03)	1 (00.50)	4 (02.05)	2 (01.03)
Low positive cohort (n=160)	154 (96.25)	1 (0.63)	1 (0.63)	1 (0.63)	2 (1.23)	1 (0.63)
Total (n=355)	338 (95.21)	3 (0.85)	3 (0.85)	2 (0.56)	6 (1.69)	3 (0.84)

Figure in parenthesis indicate percentage

Table 3: Sputum smears conversion of bacilli on different phases of DOTS Therapy.

Bacilli Found in sputum smear	At the initiation of therapy	Sputum Status at the end of specific interval							
		End of IP*		End of ext IP#		Middle of CP@		End of treatment	
		Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
Scanty	60 (17.60)	11 (18.33)	49 (81.67)	2 (3.33)	58 (96.67)	1 (1.67)	59 (98.33)	0	60 (100)
1+	95 (27.86)	17 (17.89)	78 (82.19)	3 (3.26)	92 (96.84)	2 (2.10)	93 (97.90)	0	95 (100)
2+	102 (29.91)	24 (23.53)	78 (76.47)	3 (2.94)	99 (97.06)	0	102 (100)	0	102 (100)
3+	84 (24.63)	40 (47.62)	44 (52.38)	8 (9.52)	76 (90.48)	9 (10.71)	75 (89.29)	2 (2.38)	82 (97.62)
P Value		0.00001		0.12		0.0006		0.10	

*Status at the end of IP (after 2 months of initiation of therapy); #Status at end of extended IP (after 3 months of initiation of therapy); @Status at the middle of CP (after 4 months of initiation of therapy); Figure in parenthesis indicate percentage

Table 4: Sputum smears conversion of bacilli in high positive cohort vs. low positive cohort on different phases of DOTS Therapy.

Bacilli Found in sputum smear	At the initiation of therapy	Status at the end of Specific Interval							
		End of IP*		End of ext IP#		Middle of CP@		End of treatment	
		Positive	Negative	Positive	Negative	Positive	Negative	Positive	Negative
Low grading cohort	257 (75.37)	52(20.23)	205(79.87)	8 (3.11)	249(96.89)	03(1.17)	254 (98.83)	0	257 (100)
High grading cohort	84 (24.63)	40(47.62)	44(52.38)	8 (9.52)	76 (90.48)	9(10.71)	75 (89.29)	2 (2.38)	82(97.62)
P Value		< 0.00001		0.015		0.00037		0.013	

*Status at the end of IP (after 2 months of initiation of therapy); #Status at end of extended IP (after 3 months of initiation of therapy); @Status at the middle of CP (after 4 months of initiation of therapy); ; Figure in parenthesis indicate percentage

In this study male patients (67.45%) were more than females (32.55%). The mean age of the tuberculosis patients was 43years (Table 1). Among them 95.21% patients were cured, 0.85% patients were treatment completed, 0.56% patients were declared treatment failure, 1.69% patients were transferred out, 0.85% patients were not followed up and 0.84% patients died (Table 2).

The initial sputum grading was observed for scanty, 1+, 2+ and 3+ 17.6%, 27.9%, 29.9% and 24.6% respectively. The conversion rates were for scanty, 1+, 2+ and 3+ 81.7%, 82.2%, 76.5% and 52.4% respectively at the end of the intensive phase of the treatment (Table 3). The sputum smear conversion rate was statistically significant at the end of the intensive phase and at the middle of CP of DOTS therapy respectively (p=0.0001 and p=0.0006) and it was not significant at end of extended IP as well as at the end of treatment (p=0.12 and p=0.10). It has been observed that 52.4% of mycobacterial load was reduced after intensive phase in high grading cohort whereas it was more than 79.9% reduction in low grading cohort (Table 4). Better conversion rates were observed with lesser sputum positivity grading. A patient was declared cured based on negative sputum results attained after the 7th month of treatment and on at

least one previous occasion. In this study, the cure rates were better in patients with lesser sputum smear positivity grading.

DISCUSSION

The majority of male patients (60.44%) belonged to 3rd, 4th and 5th decades with mean age of 34.5±14.1 years whereas 72.97% was female patients belonging to 3rd, 4th and 5th decades with mean age of 32.6±13.1 years. This study was with male (67.5%) preponderance. The new smear-positive cases notified in 2004 showed that maximum cases reported varies from 1st decade to 4th decade and with male preponderance according to WHO Report 2006.⁹ The male (43.91%) was less than female (67.56%) between 1st to 4th decade in the present study similar to the 3rd to 5th decade.

The present study revealed that the patients of the High Positive Cohort achieved lower conversion (52.4%) as compared to the patients in Low Positive Cohort (79.9% conversion). Similar findings (62.2% and 76.8% respectively) were reported in a retrospective study by Singla R et al¹² at LRS Institute of Tuberculosis and Respiratory Diseases, New Delhi. The present study revealed statistically significant difference in the conversion rate among the High Positive and Low Positive Cohort.

Lienhardt C et al¹³ reported sputum conversion at the end of two months in patients with initial sputum smears 1+, 2+ and 3+ were 96.2%, 85.8% and 81.8% respectively. They further served that the cure rate also decreased with a higher initial bacillary load. In this study, sputum conversion at the end of two months in patients with initial sputum smears scanty, 1+, 2+ and 3+ to be 81.67%, 82.19%, 76.47% and 52.4% respectively.

Rieder HL¹⁴ observed that sputum conversion at the end of two months of treatment among patients with initial weakly positive (scanty) sputum was 90.9%. The patients with initial moderately positive (1+ and 2+) and strongly positive (3+) sputum smear results were 77.9% and 61.7% respectively. The present study showed that sputum conversion at the end of two months of treatment among patients with initial weakly positive sputum was 81.67%. The patients with initial moderately positive and strongly positive sputum smear results were 79.19% and 52.4% respectively.

Rutta E et al¹⁵ from Tanzania (July 2001) and **Rieder HL**¹⁴ from Paris (April 1996) showed sputum conversion after the 2 month intensive phase were 88.0% and 75.0% respectively. The present study corroborates the findings of **Rieder HL**¹² and **Rutta E et al.**¹⁵

Lienhardt C et al¹³ from Gambia (September, 1998) observed sputum smear conversion at the end of 2 months after the start of treatment was 90.0% and it was more likely to occur if the initial bacterial load in the sputum was low (scanty, 1+, 2+). The present study is comparable with **Lienhardt C et al.**¹³

Rajpal et al¹⁶ from New Delhi (2002) revealed that patients with 3+ sputum smear grading not only required extension of treatment in the intensive phase more often than those with scanty, 1+ or 2+ grading but also had significantly higher failure rate. The present study showed that patients with high positive cohort (3+) had higher failure rate and needed extension of treatment after completion of Intensive phase.

Singla R et al¹⁷ from New Delhi in (2003) concluded that among age group ≥ 41 years, presence of numerous bacilli on initial sputum smear examination, and multiple cavitory disease were the significant factors associated with persistent sputum positivity at the end of 2 months of treatment ($P < 0.0001$). The present study revealed that patients with 3+ sputum smear grading required extension of treatment in the intensive phase than those with scanty, 1+ or 2+ grading.

Zhao FZ et al¹⁸ from China (1997) revealed that 95% patients' sputum showed conversion in the third month of treatment. They concluded sputum

conversion during the third month of treatment is an important predictor of treatment success, failure to convert predicts treatment failure.

In a study done by **Singla R et al**¹² from New Delhi (2005), sputum conversion rates among patients graded as 3+ and rest of the patients at the end of two months were 62.2% and 76.8% respectively ($p < 0.0001$), and at the end of three months were 81.3% and 89.5% respectively ($p < 0.0001$). They concluded that smear positive patients with heavy bacillary load showed statistically significant poor sputum conversion rates at two and three months and higher failure rates as compared to patient with lesser bacillary load. The present study is comparable with **Singla R et al**¹² study.

Baruwa P et al¹⁹ (April 2005) did a study which showed sputum conversion of 84% after 2 months intensive phase. In this study sputum conversion was also corroborating with the study of **Baruwa et al.**

CONCLUSION

The conversion rate of sputum is associated with initial sputum grading. There is undeniable evidence that patients with higher sputum grading have an increased risk of poor outcome than their counterparts with lower smear grading. The conversion rate and success rate were also reduced with increased sputum grading. It is therefore recommended that early identification of patients who may have an increased risk of a poor outcome such as high sputum smear grading should be reduced with interventions, such as treatment modification and closer monitoring is needed to reduce the potential of poorer treatment outcomes.

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