

Analysis of Risk Factors Affecting Sputum Conversion at the End of Intensive Phase Under DOTS for Treatment of Pulmonary Tuberculosis

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ABSTRACT

Introduction: Microbiologically confirmed pulmonary tuberculosis patients under Revised National Tuberculosis Control Programme (RNTCP) are treated with a 6-month short-course chemotherapy (SCC) regimen irrespective of co-morbid conditions. The aim of present study was to determine the time taken for SCC conversion with standard current treatment with anti-tubercular drugs and analysis of risk factors if any delaying it. We undertook this prospective study to compare sputum conversion rates (smear) at the end of intensive phase (IP) of Category regimen.

Material and methods: was a prospective study which was conducted for a period of eleven months from August 2018 to June 2019 at Department of Respiratory Medicine, K.N Chest Hospital, S.N Medical College, Jodhpur Rajasthan India. Patients visiting Department of Respiratory medicine and who were diagnosed as pulmonary tuberculosis by sputum smear examination were included in study.

Result: Sputum smear-positive patients are infectious to close contacts as well as to community as they continue to expel bacilli for a variable period of time after initiation of DOTS regimen. Most patients undergo sputum conversion by the end of 3rd month. Patients who have predominant cavitary disease in radiology, high smear grading before treatment, a prior history of DS/DR tuberculosis are more likely to have delayed sputum smear conversion.

Conclusion: There need to mandate DST at the starting of DOTS in line with latest RNTCP guidelines to prevent the development of MDR strains and failures. Also there is a strong need to constitute strong infection control measures till patients are labelled as noninfectious.

Keywords: Pulmonary Tuberculosis, Revised National Tuberculosis Control Programme, Short Course Chemotherapy, Sputum Smear Conversion, Directly Observed Treatment Short Course.

INTRODUCTION

Globally tuberculosis is one of the top 10 causes of death and a leading cause from a single infectious agent (above HIV/AIDS). Large battery of people fall sick with TB each year. In year 2017, TB caused an approximate of 1.3 million deaths among HIV-negative people and there were an additional 300000 deaths from TB among HIV-positive people.¹ There is a upfront uproar of TB after HIV with increased mortality and drug resistance. To fight this calamity, India adopted WHO "TB control strategy".² Implementation of Directly observed therapy short course (DOTS) is one the vital move

taken by RNTCP to control and treat cases of tuberculosis. Effective implementations of diagnostic facilities, control measures, and treatment modalities are part of this strategy. One of the key components in this strategy is diagnosis through a quality assured network microscopy centers.

Sputum positive patients are a source of infection and should be started on DOTS with two months of intensive phase (IP) and four months of continuation phase (CP). Sputum conversion by effective DOTS is evaluated by sputum smear conversion [SSC] which is important parameter for treatment success. More than 80 percent patients are sputum converted by end of 2nd month.³

Multiple factors may delay SSC like Diabetes mellitus, HIV, initial bacillary load at diagnosis, hepatic disorder, old age, extent of lung involvement, cavitary lesions and MDR-TB.^{4,5} Studies available on factors affecting SSC in India are few and limited. Present study was done assess time taken for smear conversion and evaluate factors that delay smear conversion. Smear conversion is defined as New smear-positive PTB cases who have become smear negative after taking anti- TB treatment and are no longer infectious

MATERIAL AND METHODS

It was a prospective study which was conducted for a period of eleven months from August 2018 to June 2019 at Department of Respiratory Medicine, K.N Chest Hospital, S.N Medical College, Jodhpur Rajasthan India. Patients visiting Department of Respiratory medicine and who were diagnosed as pulmonary tuberculosis by sputum smear examination were included in study. Two sputum specimens

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were collected from the patients [Spot and early morning] and Ziehl – neelsen [Zn] staining was done and smear positive were graded as per standard RNTCP guidelines. Informed consent was obtained from all the patients enrolled in the study. The clinical, demographic and social profiles of patients were assessed at time of inclusion in study. Patients not compliant to DOTS regimen, cases of extra pulmonary tuberculosis, patients with lost to follow up, <18 years were excluded from the study.

RESULTS

In present prospective study which was conducted for a period of eleven months from August 2018 to June 2019 study, a total of 75 patients were enrolled which included 44 (59%) males and 31 (41%) females.

Result tables are as follows:

Sex	No. of cases	Percentage
Male	44	59%
Female	31	41%
Total	75	100%

Table-1: Distribution of cases according to sex pattern (N-75)

Age Group (Yrs)	No.
<20	1
21-30	19
31-40	29
41-50	18
51-60	5
>60	3

Most of the patients were in 21 to 40 years of age group

Table-2: Age-Groups and Relation to Gender Profile

Group	Total	
	No.	%
Smokers	50	66.6
Non-Smokers	15	20
Total	75	100
Alcoholic	20	26.6
Non-Alcoholic	55	73.3

Table-3: Distribution of cases according to smoking/alcohol habits

Lung Involvement and Associated disease	No.
Lung Involvement	
U/L	25
B/L	50
HIV	
Reactive	6
Non-Reactive	69
DM	
Yes	21
No	54
Cavity	
Present	39
Absent	36

Table-4: Lung Involvement and Associated Disease

S. No.	Symptoms	No. of cases
1	Fever	72
2	Cough with expectoration	68
3	Hemoptysis	45
4	Loss of appetite	56

Table-5: Spectrum of Respiratory and Constitutional symptoms

	No. of cases
3+	20
2+	18
1+	20
Scanty	7

Table-6: Grading of smear by microscopy

Time period	Positives	Negatives	%age Conversion
By 4th week	48/75	27	36
By 8th week	29 /75	46	61
By 12th week	17 /75	58	77
By 16th week	6 /75	69	91
By 20th week	2 /75	73	97

Table-7: Sputum conversion rates by microscopy.

Mean age in study was 36.41 years Table -1. Most common age group (Table-2) affected in the study was between 31-40 years. The most common clinical symptom (Table-3) of presentation was fever (98.67%) followed in order by a cough with expectoration (82.67%), loss of appetite (74.67%) and hemoptysis (64%). 6 cases (8%) in the study were HIV co-infected (Table-4), 21 cases (28%) were diabetic. Table 5 shows spectrum of respiratory and constitutional symptoms. Table 6 shows grading of smear by microscopy. The median time taken for sputum conversion (Table-7) for cases in the study was by the end of 4th week [day 28]. In present study by end of 4th week, sputum smear conversion (SSC) was seen in 27 cases (36%). By the end of 12th week in our study 58 cases (77.33%) were sputum negative at the end of 20th week, 2 cases (2.67%) remained both sputum and culture positive. All the cases which remained positive were HIV seropositive 4 cases which remained sputum and culture positive until 20th week are HIV seropositive with bilateral involvement of lung with cavitory lesions

DISCUSSION

The open cases of TB are a constant source of infection in the community. In a developing country like India TB adds to the socioeconomic burden of the country.² Timed recognition of such high risk cases is essential in introducing strict vigilance so as to minimise spread of infection among the contacts and also hasten the process of smear negativity by monitored treatment. It is of prime importance to understand and recognise factors that affect rate of smear conversion amongst patients. Many studies are conducted to identify such factors^{2,4}

Timed follow-up of pulmonary tuberculosis cases on DOTS, by sputum smears and cultures, are thought to be one of the major and reliable predictors of treatment response. Prior

studies have shown that non-conversion of sputum smear positive patients at the end of intensive phase of treatment is strongest evidence for treatment failure.^{6,7}

In present study, we highlighted the time taken for smear conversion as a measure of non-infectivity and factors that delay this in patients on DOTS treatment

In present study follow up was done at end of 4th, 8th, 12th, 16th and 20th week because, patients treated under DOTS would be labelled as “treatment failure” if they were smear-positive at the end of 5th month of treatment. Out of total 75 cases, 97.33% (71/75) had a favorable treatment outcome as they became smear and culture negative by the end of 20th week. This is above target cure rate of 85% in Millennium Development goals.⁸ The median time taken for smear conversion was 28th day .

Out of 75 patients, two remained sputum positive until 20th week indicating the possibility of

MDR-TB and were shifted further evaluation for MDR Tb, while 71 patients completed CAT-I treatment. Patients who were smear by the end of 20th week were considered successfully cured. Smear conversion started increasing gradually from 3rd and 4th week of starting of DOTS regimen. By the end of 16th week, 91.33% of cases turned sputum negative; this is comparable to national average of 90%. This is similar to the findings of Long et al and Pachas et al who reported in their studies the 93% of SSC by the end of 16th week.^{8,9}

In present study out of total 75 patients two patients remained sputum positive till end of 20th week of treatment and was given anti-tubercular drugs again and were evaluated further. The possible reason for this may be multidrug resistance tuberculosis which was not undertaken in our study which is a limitation. Based on the findings of this study, and depending on resources available, Drug susceptibility testing (DST) should be carried out on all such patients who continue to remain smear-positive at the end of the 2nd month or 3rd month and should not be delayed until the end of 5th month. This would prevent spread of MDR-TB in case the continued smear positivity is due to drug-resistant strains. This is especially important in a country like India with high rates of primary drug resistance.^{10,11} Analysis of risk factors causing delayed sputum and culture conversion was observed in patients with high initial bacillary load (3+), hepatic disorder, HIV positivity and bilateral lung involvement with cavitory lesions. DM was not a significant risk factor in delayed sputum conversion. These findings are similar to findings in studies done by Gopi PG et al,

Holtz TH et al and Guler M et al where high sputum bacillary load and cavitory lesions were significant risk factors in delayed conversion of sputum smear.^{12,13,14}

Lung cavities contain millions of TB bacilli and bilateral involvement of lung are associated condition which causes high bacillary load and leads to development of drug-resistant strains. HIV status of patient is a risk factor in many studies; however in present study 6 cases were positive and completed the study. Two of the cases were sputum and culture positive by

end of 20th week. Both had bilateral cavitory lesions which might have delayed conversion. Patients with TB who are co-infected with HIV are at increased risk of developing MDR . Rest of the six cases had delayed sputum conversion which may be cavitory lesions and HIV coinfection. Hence persons diagnosed with HIV in TB infection should undergo DST to screen MDR cases to modify the regimen if necessary based upon DST.

CONCLUSION

This article highlights the fact that sputum smear-positive patients are highly infectious to close contacts as well as to community were they reside as they continue to expel bacilli for a variable period of time after initiation of DOTS regimen. Most patients undergo sputum conversion by the end of 2nd month.

Patients who have cavitory disease, high pre-treatment smear grade, a past history of tuberculosis or MDR-TB are more likely to remain smear positive for longer periods of time.

Hence there is a utter need to mandate DST at the starting of DOTS in line with latest RNTCP guidelines to prevent the development of MDR strains and failures. Also there is a strong need to constitute strong infection control measures till patients are labelled as noninfectious.

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