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Original Research Article

Relationship between Sputum Smear Grading and Smear Conversion Rate and Treatment Outcome in the Patients of Pulmonary Tuberculosis Undergoing Dots in Kerala -A Prospective Cohort Study

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Abstract

Background: The SCR is an operational indicator for the DOTS strategy of Revised National Tuberculosis Control Programme (RNTCP) in india. The present study was undertaken to determine the relationship between sputum smear grading and smear conversion rate among the category I smear positive pulmonary tuberculosis patients undergoing DOTS. ***Methods:*** A prospective cohort study was carried out among category I pulmonary smear positive patients registered at the DOTS centres of District TB centre Karuvelipady, Government hospital Ernakulam ,Government hospital Paravur. The patients with pre-treatment sputum grading 3+ were placed in High positive cohort (HP cohort) and those with pre-treatment sputum grading as 2+,1+ and scanty were placed in Low positive cohort (LP cohort) were followed periodically at two months (end of Intensive phase),at three months (after one month extension of Intensive phase),at two months of Continuation Phase and then at the end of the treatment to record the sputum AFB result and treatment outcome as per the RNTCP guidelines. Accordingly, a total of 397 category I patients with 213 in HP cohort and 184 LP cohort were enrolled in the study during November 2016 to January 2017. Data were analyzed using Medcalc Online calculator. ***Results:*** After two months (end of the intensive phase), SCR was 53.52% (114 of 213) among the High Positive and 69.56% (128 of 184) in the Low Positive cohort (p-0.001).After three months (one month's extension of intensive phase),cumulative SCR was 74.17% (158 of 213) in the High positive and 84.25% (155 of 184) in the Low Positive cohort(p-0.01).Cure rate was 68.07% (145 of 213) in the High Positive and 77.71% (143 of 184) in the Low Positive cohort. Default rate was 23% (49 of 213) in the High Positive and 12.5% (23 of 184) in the Low Positive cohort. Failure rate was 3.28% (7 of 213) in the High positive and 4.89% in the Low positive Cohort (9 of 184).Twelve patients (5.63%) died in HP Cohort, nine patients in LP Cohort (p-0.23). Treatment outcome was further compared among the patients according to their sputum status achieved at two and three months of the treatment after ignoring their initial sputum status. The cure rates for the patients who converted at two months was 92.56% (224 of 242) and for those who did not convert at two months, was 55.65% (64 of 115) (p- 0.00001). Similarly, the cure rate for the patients who converted at three months was 78.04% (64 of 82) and for those who did not convert at three months was 0% (74) (p-0.00). ***Interpretation:*** Patients with higher grades of sputum positivity at the beginning of the treatment have significantly lower SCR at the end of intensive phase and even after extending the intensive phase for one month. Hence, they are likely to remain infectious for a longer duration and continue to transmit infection in the community. Therefore, these patients demand to have more stringent self-precautionary measures to break the chain of infection in the community. The SCR at two months and three months as an operational indicator should be given more importance rather than being practised only as a documentation and academic exercise.

Keywords: DOTS, Pulmonary Tuberculosis, Sputum Smear Grading, Smear Conversion Rate, Treatment Outcome.

INTRODUCTION

The Directly Observed Treatment Short course (DOTS) strategy along with the other components of the Stop TB strategy, implemented under the Revised National Tuberculosis Control Programme (RNTCP), is a comprehensive package for TB control in India. Sputum AFB microscopy remains the corner stone for the success of DOTS strategy worldwide as it plays a fundamental role in case detection, diagnosis, categorization and follow up. In the DOTS programme, smear is graded according to WHO recommendations for RNTCP as 3+,2+,1+,scanty or negative based on the number of AFB seen in the sputum smear [1].

Sputum smear conversion at the end of the intensive phase of treatment is used as an important early predictor of treatment success .WHO continues to recommend performing smear microscopy at this stage because a positive smear should trigger an assessment of the patient, as well as additional sputum monitoring. The sputum conversion results are used both for management of patients and for monitoring programmed performance [2].

The objective of study was to determine the relationship between pre-treatment sputum smear grading (as 3+,2+,1+ and scanty) and SCR and its relative importance in predicting the treatment outcome of the tuberculosis patients registered under DOTS.

MATERIALS AND METHODS

A prospective cohort study was carried out among category I pulmonary smear positive patients registered at the DOTS centres of District TB centre Karuvelipady, Government hospital Ernakulam, Government hospital Paravur, Ernakulam district .Study protocol was presented to ethics committee, after obtaining approval from ethics committee, the study commenced. The patients with pre-treatment sputum grading 3+ were placed in High positive cohort (HP cohort) and those with pre-treatment sputum grading as 2+,1+ and scanty were placed in Low positive cohort (LP cohort) for analysis. Accordingly, a total of 397 category I patients with 213 in HP cohort and 184 LP cohort were enrolled in the study during November 2016 to January 2017.

Sputum results and treatment outcome were recorded from laboratory records and patient's treatment cards.

All the study subjects were interviewed using a separate proforma. Subsequent visits to the DOT centres were made to collect the information on sputum results at two months IP, at three months IP (extended IP), at two months of continuation phase (CP) and then at completion of the treatment. The outcome variables of the study, SCR and Treatment outcome were defined as per operational guidelines under the RNTCP.

Data was analyzed using Medcalc Online calculator. Unpaired t test, Chi square test were applied. P- value below 0.05 was considered to be statistically significant.

RESULTS

Socio-demographic information such as age, sex is summarized in Table-1. The mean age of the patients in HP cohort was 49.57 years (SD± 13.2) and that for the LP cohort was 49.25 (SD± 15.72) years. Majority of the patients in both the cohorts was from the most productive age group of life ie, between 31-70 years of age. The percentage of males was slightly more than the female patients in both the study cohorts.

Being a prospective cohort study, the number of the patients varied at each stage of the treatment due to loss to follow up as default, death, failure. In the HP cohort, 49 patients defaulted (five in IP, ten in Extended IP and thirty four patients in CP). Twelve patients died (one in IP, two in Extended IP and four patients in CP). Seven patients were labelled as failures because of persistently positive sputum at two months completion of CP, therefore shifted to the category II. In the LP cohort, twenty three patients defaulted (four in IP, eight in Extended IP and eleven in CP). Nine patients died (two in IP, five in Extended IP, two in CP).Nine patients were labelled as failures because of persistently positive sputum at two months completion of CP, therefore shifted to the category II.

Table-1: Socio-demographic details of study subjects of high positive and low positive cohort

characteristics	High positive cohort n=213 (%)	Low positive cohort n =184(%)	P value
Age			
<16	0(0.0)	1(0.54)	0.8303
16-30	21(9.85)	29(15.76)	
31-50	88(41.31)	60(32.6)	
51-70	98(46)	85(46.19)	
>70	6(2.81)	9(4.89)	
GENDER			
MALE	175(56)	138(44.08)	0.8777
FEMALE	37(44.04)	45(53.57)	

Table-2: Smear conversion rate in the high positive cohort vs low positive cohort at two months of ip and at three months of IP

Patients initated on DOTS	High positive cohort (N=213)	Low positive cohort (N=184)	P value
Smear conversion rate at 2 months of IP n (%)	114(53.52)	128(69.56)	0.0011
Smear conversion rate at 3 months of IP n (%)	44(20.65)	27(14.67)	0.1215
Cumulative n (%)	158(74.17)	155(84.25)	0.0143

Table-3: Treatment outcome of high positive cohort vs low positive cohort

Patients initated on DOTS	Cured n (%)	Defaulted N (%)	Failure n (%)	Died n (%)
High positive cohort (N=213)	145(68.07)	49(23)	7(3.28)	12(5.63)
Low positive cohort(N=184)	143(77.71)	23(12.5)	9(4.89)	9(4.89)
Total(N=397)	288(72.54)	72(18.13)	16(4.03)	21(5.28)
P value	0.237			

Table-4: Treatment Outcome Converted Cohort vs Not Converted Cohort at two months (ignoring pre-treatment sputum smear status)

Patients initated on DOTS	Cured n (%)	Defaulted N (%)	Failure n (%)	Died n (%)
Converted at two months (N=242)[a]	224(92.56)	14(5.78)	3(1.23)	1(0.4)
Not converted at two months (N=115)[b]	64(55.65)	59(51.30)	13(11.30)	19(16.52)
Total (N=357)	288(80.67)	73(20.44)	16(4.48)	20(5.60)
P value	0.00001			

Table-5: Treatment Outcome of Converted Cohort vs not Converted Cohort at three months ie, after one month's extension of Intensive Phase (ignoring pre-treatment sputum smear status)

Patients initated on dots	Cured n (%)	Defaulted N (%)	Failure n (%)	Died n (%)
Converted at two months (N=82)[c]	64(78.04)	14(17.07)	4(4.87)	0(0.0)
Not converted at two months (N=74)[d]	0(0.0)	46(62.16)	9(12.16)	19(25.67)
Total (N=156)	64(41.02)	60(38.46)	13(8.33)	19(12.17)
P VALUE	0.00			

Being a prospective cohort study, the number of the patients varied at each stage of the treatment due to loss to follow up as default, death, failure. In the HP cohort, 49 patients defaulted (five in IP, ten in Extended IP and thirty four patients in CP). Twelve patients died (one in IP, two in Extended IP and four patients in CP). Seven patients were labelled as failures because of persistently positive sputum at two months completion of CP, therefore shifted to the category II. In the LP cohort, twenty three patients defaulted (four in IP, eight in Extended IP and eleven in CP). Nine patients died (two in IP, five in Extended IP, two in CP). Nine patients were labelled as failures because of persistently positive sputum at two months completion of CP, therefore shifted to the category II.

As shown in Table-2, SCR after two months of IP showed statistically significant difference between two cohorts (HP Cohort -53.52%) and LP Cohort -69.56%); p value 0.001). The cumulative SCR after extended IP was also significantly different between the two cohorts (HP Cohort-74.17% and LP Cohort -84.25%; p value 0.01).

Treatment outcome as shown in Table-3, did not show any significant difference between the two cohorts (p value -0.23) but, comparatively higher proportion of patients were defaulted (23%; 49 of 213) in HP Cohort than in the LP Cohort (12.5%; 23 of 184).

In Tables 4 and 5, treatment outcome was further compared among the patients according to their sputum status achieved after two and three months of treatment after ignoring their initial sputum status. For this purpose, patients were again divided as Converted and Non- converted cohorts at two months and similarly at three months. It may be noted that only patients whose sputum result was available at two and three months, were analyzed for their treatment outcome. It was found that the cure rate was significantly lower for the patients who failed to achieve smear conversion at two and three months. This finding further reiterates that SCR at two and three months is a very strong determinant of treatment outcome of patients.

DISCUSSION

Pre-treatment sputum smear grading is a direct measure of number of bacilli present in a smear and thus severity of disease which may affect the smear conversion and final treatment outcome. There are studies available which highlighted the importance of initial sputum smear grading and revealed that higher grades of smear positivity result in delayed smear conversion poor treatment outcome.

The present study revealed that the patients of the HP Cohort achieved lower conversion and cure rates as compared to the patients in LP Cohort. Compared with Simmi Tiwari *et al*., [3] study smear conversion rate at the two months and three months (57.9% and 85.2%), LP Cohort group showed 69.56% &84% smear conversion at the end of 2 months & 3 months and this rate also less in comparison with Simmi Tiwari *et al.*, study 71.6% & 92.3%. Treatment outcome did not show any significant difference

between the two cohorts (p value-0.631) but, comparatively, higher proportion of patients were failures (11.2%; 19 of 169) in the HP Cohort than in the LP Cohort (6.5%; 11 of 169). Rupak Singla *et al*., reported smear conversion at the end of two months 62% & 76.8%; Smear conversion at the end of three months 81.3% and 89.5% respectively (p.0.001) [4].

Singla R. *et al.*, reported SCR among the patients graded as 3+ and (combined graded 1+,2+) at the end of the IP as 62.2% and 76.8% respectively and at the end of three months as 81.3% and 89.5% respectively. The cure rate among these patients were 76.6% and 85.1% respectively and failure rates were 7.7% and 4.5% respectively. However, the present study did not show statistically significant difference in the cure rate and failure rate among the HP and LP Cohort [5]. Lienhardt *et al*., reported sputum conversion at the end of two months in patients with initial sputum smears 1+,2+,and 3+ to be 96.2%,85.8% and 81.8%, respectively. They further observed that the cure rate also decreased with a higher with a higher initial bacillary load. Another study from Saudi Arabia reported numerous bacilli on pre-treatment sputum smear examination as an independent risk factor associated with persistent sputum smear positivity at the end of two months of treatment using DOT under national programme conditions [6].

Similarly, in a refugee camp in Thailand under DOTS, Rieder *et al*., observed that sputum conversion at the end of two months of treatment among patients with initial weakly positive sputum to be 90.9%. It was 77.9% and 61.7% among patients with initial moderately positive and strongly positive sputum smear results, respectively [7].

Findings from the present study reiterate the fact that the patients who have higher grades of sputum positivity at the beginning of treatment have significantly lower conversion rates at two and at three months even though the overall treatment outcome did not show any significant difference with respect to sputum grading. The importance of SCR as an operational indicator can be further understood by the fact that the patients who remain smear positive (not converted) at two and three months, achieve significantly lower cure rates in comparison to those who get converted at two and three months [8].

So, the pre-treatment sputum smear grading can help pinpoint a group of patients who may require an extension of intensive phase of treatment more often and their treatment outcome is likely to be worse than that of others. SCR at two and three months can help a physician in deciding the necessary investigations to be done at the earliest to detect other co-morbid conditions and go for sputum culture and sensitivity to rule out drug resistance, if any. The pre-treatment higher bacillary load and consistent smear positive status at two and three months of IP is found to be a significant risk factor for developing Multi Drug Resistant Tuberculosis (MDR TB) according to a study done in Eritrea [9]. Similarly the study conducted at the All India Institute of Medical Sciences by J. N Pande *et al*., reported the pre-treatment higher bacillary load to be a risk factor for MDR TB [10]. Understandably, the delayed and poor SCR of patients with higher grades at the beginning of treatment continue to transmit infection in the community for a longer duration of time and hence contribute to the prevalence pool of infective tuberculosis in the community. These patients need to be motivated to take self-precautionary methods to prevent the spread of infection in the community.

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