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Original Article

Factors Affecting Sputum Smear Conversion Time in Newly Diagnosed Pulmonary Tuberculosis Patients

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Abstract

Background: Patients having tuberculosis are registered in the TB DOTS program for their treatment. During the treatment sputum samples are sent periodically to the laboratory to check treatment efficacy. Usually after two months of treatment sputum smear becomes negative but presence of multiple cavities in the lung, bacillary load, diabetes mellitus and tobacco smoking, slows the sputum smear conversion time.
Objectives: To determine the factors affecting sputum smear conversion time in newly diagnosed pulmonary tuberculosis patients.
Study design, settings and duration: This cross sectional, analytical study was done by Pakistan Medical Research Council, TB Research Centre in collaboration with Institute of TB and Chest Medicine King Edward Medical University/Mayo Hospital, Lahore from April 2013 to March, 2014
Patients and Methods: All newly diagnosed pulmonary tuberculosis patients who were registered and given treatment by the DOTS program were included in the study. All patients underwent sputum smear microscopy along with Complete Blood Count and ESR at the time of enrollment. The patients were followed for next 6 months while on treatment. Sputum samples were tested at 2nd and 6th month to check the sputum conversion rate and indirectly to see the efficacy/compliance to treatment.
Results: A total of 400 patients were enrolled with slightly more males (52%) as compared to females (48%). Smear became negative within two months of starting treatment in 85.7% patients while in 14.2% it remained positive at 2nd and 6thmonths of therapy. There were more females (10.7%) whose sputum smear did not became negative as compared to males (3.5%). Predominant factors affecting sputum smear conversion were low resistance, raised initial bacillary load, decreased hemoglobin level, and long duration of symptoms at the time of diagnosis.
Conclusion: Factors like low resistance, high initial bacillary load and decreased hemoglobin levels affect the sputum smear conversion and should be addressed while assessing efficacy of anti-tuberculosis treatment.
Key words: Tuberculosis, anti tuberculosis treatment, Ziehl Neelsen stain, Acid Fast Bacilli.

Introduction

Tuberculosis (TB) is a major public health problem throughout the world. In 2005, there were estimated 8.8 million new cases of TB accounting for1.6 million deaths worldwide[1]. The South-East Asia region reported 4.88 million TB cases, and carries one-third of the global burden of TB[2]. Pakistan ranks sixth on the list of 22 high-burden tuberculosis (TB) countries in the world. In 2007, an estimated 297,108 people in Pakistan developed TB and its incidence in Pakistan is 181/100,000 population[3,4]. The main source of tuberculosis infection is the patient with active pulmonary TB whose sputum contains tubercle bacilli which are transmitted to others via air[5,6]. Factors associated with infectivity of the tuberculosis include bacterial load, severity of coughing, proximity to the patient and the duration of anti-TB therapy[6]. The most widely accepted measure of treatment response in patients with pulmonary TB is the disappearance of acid-fast bacilli (AFB) from both sputum smear and culture. In addition, various serological markers have been evaluated as indicators of disease activity, but their clinical usefulness remains uncertain[7]. Several factors have been indicated that affect the sputum smear conversion time in patients with active tuberculosis. These factors include, bacterial load, HIV co-infection, diabetes, age, infection from multi-drug resistant strains, development of drug resistance, presence of cavitation in lungs and gender[8,9].

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Aim of this study was to see the factors affecting sputum smear conversion time among newly diagnosed tuberculosis patients.

Patients and Methods

This cross sectional, analytical study was undertaken by PMRC TB research center in collaboration with Institute of TB and Chest Medicine, King Edward Medical University/Mayo Hospital, Lahore from April, 2013 to March, 2014. Semi-structured questionnaire was used to collect information regarding medical history, characteristics of household, demography, social characteristics along with BCG vaccination, weight, height and clinical symptoms.

As Mayo Hospital is located in the center of Lahore, therefore patients come from all over Lahore. About 5cc blood was drawn from each patient who also submitted their sputum samples at 2ndand 6thmonth after the initiation of ATT and at the completion of treatment. Complete blood count and ESR of all patients were done at the start of ATT, at 2nd months and on completion of ATT.

After taking written consent from 400 newly diagnosed confirmed pulmonary TB patients who were starting their anti-tuberculosis treatment (ATT) were enrolled in the study.

Results

A total of 400 newly confirmed (smear positive) tuberculosis patients were included in the study. There were 52% males and 48% females. Most of the patients were married (66.5%), illiterate (62%) and had the family income of less than Rs. 20,000 per month (77.5%). History of contact with TB was present in 53% patients. The demographic characteristics of patients are presented in Table-1.

Following treatment, 343 (85.7%) patients became smear negative within 2 months of treatment while 57 (14.25%) patients remained smear positive after 2nd and 6thmonths. Females were more prone to sputum smear non conversion 43 (10.75%) when compared with males 14 (3.5%). Details of relationship between sputum smear conversion times with relation to gender are given in the Table-2.

Patients with high bacillary load were more susceptible to non-conversion as compared to those with low load. Only 10 (9.0%) subjects having 1+ bacillary load did not convert while 29 (21.0%) having 3+ bacillary load did not convert (Table-2).

Patients showing sputum smear conversion had lower ESR at the time of diagnosis which kept on decreasing with the continuation of treatment. In patients showing sputum smear non-conversion, the ESR was higher at the time of start of treatment and it kept on increasing during therapy (Table-3).

Table 1: Demographic characteristics of the study participants.

Character	*Description*	*N*	*%*
Gender	Male	208	52.0
	Female	192	48.0
Marital status	Married	266	66.5
	Unmarried	134	33.5
History of contact	Yes	212	53.0
	No	188	47.0
BCG scar	Yes	274	68.5
	No	126	31.5
Educational status of patient	Illiterate	248	62.0
	Primary	104	26.0
	Middle	26	6.5
	High school	10	2.5
	Intermediate	4	1.0
	Graduation	8	2.0
Economic status	< 10000	41	10.2
	10000 – 20000	310	77.5
	20000 – 40000	47	11.8
	40000 – 60000	2	0.5

Table 2: Sputum smears conversion and its relation with the bacillary load and gender.

Category		*Converted*	*Not Converted*		*Total*
		Negative (N=343) N (%)	*1+ (N=43) N (%)*	*2+ (N=14) N (%)*	*400*
Initial Bacillary Load	1+	111(92.0)	10(8.0)	0	121
	2+	118(87.0)	10(7.0)	8(6.0)	136
	3+	114(80.0)	23(16.0)	6(4.0)	143
Gender	Male	194(56.6)	9(20.9)	5(35.7)	208
	Female	149(43.4)	34(79.1)	9(64.3)	192

Table 3: Sputum smears conversion and its relation with the erythrocyte sedimentation rate.

	Category	*Converted*	*Not Converted*		*p-value*
		Negative (N = 343)	*1+ (N= 43)*	*2+(N= 14)*	*ANOVA*
		A	*B*	*C*	
ESR levels mm/hour	Baseline	44.87 ± 29.50	85.30 ± 23.95 ^{A}	111.14 ± 9.97 ^{AB}	< 0.001
	2 months	13.59 ± 8.44	46.30 ± 27.75 ^{A}	78.71 ± 33.09 ^{AB}	< 0.001
	6 months	7.29 ± 2.96	51.44 ± 27.77 ^{A}	63.36 ± 34.27 ^{AB}	< 0.001

Test is adjusted for all pairwise comparisons within a row of each innermost sub-table using the Bon ferroni correction. Results are based on two sided test assuming equal variance with significance level 0.05 for each significant pair the key of smaller category appears under the category with larger mean.

Table 4: Sputum smear conversion and its relation with hemoglobin level.

	Category	*Converted*	*Not Converted*		*p-value*
		Negative (N = 343)	*1+ (N= 43)*	*2+(N= 14)*	*ANOVA*
		A	*B*	*C*	
Hemoglobin levels g/dl	Baseline	11.82 ± 1.84	11.93 ± 5.53	11.01 ± 2.59	0.479
	2 months	12.25 ± 1.54 [BC]	9.45 ± 1.46	9.96 ± 2.58	< 0.001
	6 months	13.25 ± 1.14 [BC]	9.26 ± 1.47	9.67 ± 2.89	< 0.001

Test is adjusted for all pairwise comparisons within a row of each innermost sub-table using the Bon ferroni correction. Results are based on two sided test assuming equal variance with significance level 0.05 for each significant pair the key of smaller category appears under the category with larger mean.

Table 5: Sputum smears conversion and its relation with the duration of symptoms.

Duration of symptoms in term of Days.	*Converted*	*Not Converted*		*p-value*
	Negative (N = 343)	*1+ (N= 43)*	*2+(N= 14)*	*ANOVA*
	A	*B*	*C*	
Duration cough	10.20 ± 8.47	18.13 ± 14.51 [A]	11.10 ± 8.09	< 0.001
Duration expectoration	9.87 ± 7.88	12.47 ± 14.51 [A]	11.14 ± 8.09	< 0.001
Duration fever	10.09 ± 8.51	10.39 ± 14.51 [A]	10.11 ± 8.09	< 0.001
Duration chest-pain	9.97 ± 8.21	16.47 ± 14.51 [A]	11.12 ± 8.09	< 0.001
Duration weight loss	9.56 ± 7.40	14.47 ± 14.5[AC]	12.14 ± 8.09	< 0.001
Duration Fatigue.	9.55 ± 7.43	16.68 ± 14.5[AC]	13.17 ± 8.09	< 0.001
Duration breathlessness	9.45 ± 7.53	14.54 ± 14.51 [AC]	10.14 ± 8.09	< 0.001
Duration anorexia	9.35 ± 7.55	17.52 ± 14.51 [AC]	11.17 ± 8.09	< 0.001

Test is adjusted for all pairwise comparisons within a row of each innermost sub-table using the Bon ferroni correction. Results are based on two sided test assuming equal variance with significance level 0.05 for each significant pair the key of smaller category appears under the category with larger mean.

All patients at the time of diagnosis showed decreased hemoglobin level but these levels improved in those patients who showed conversion while levels further decreased in those whose sputum smear did not convert (Table-4).

Sputum smear conversion time showed that those who had longer duration of symptoms at the time of diagnosis had higher chance of sputum smear non-conversion (Table-5).

Results are based on two-sided tests assuming equal variances with significance level 0.05. For each significant pair, the key of the smaller category appears under the category with larger mean.

Discussion

In present study female gender, patients having high bacillary load, high baseline ESR, those showing little or no improvement in hemoglobin levels following treatment and those who had longer duration of symptoms at the time of diagnosis had higher chance of remaining sputum positive as compared to the other group.

Tuberculosis is a deadly infectious disease which made a dramatic comeback, therefore in 1993 World Health Organization declared it a global emergency[10,11]. According to a report, Pakistan contributes about 44% of tuberculosis burden in the Eastern Mediterranean Region[12].

In present study female gender was the first prominent factor found associated with poor sputum smear conversion. This finding is different from another study which showed males more prone to sputum smear non-conversion[13].

In the present study, sputum smear non conversion rate was directly associated with the initial bacillary count of the patient at the time of diagnosis, this is in agreement with other study that reported delayed sputum smear conversion time in high bacillary count patients[14].

ESR is another prominent diagnostic and prognostic indicator of TB[8]. In the present study ESRs value as prognostic marker showed improvement in those who responded to treatment and showed smear conversion while in non convertors the ESR kept on increasing despite continuation of treatment.

Improvement in hemoglobin levels subsequent to successful TB treatment has been reported by other workers[15] and same was seen in the present study where patients having successful sputum smear conversion showed gradual increase in the hemoglobin levels as compared to those who did not convert. This group indeed showed gradual decrease in the level of the hemoglobin.

Longer duration of symptoms was found associated with the lower sputum smear conversion rate as compared to the patients with less duration of the symptoms at the time of diagnosis and same was reported by other workers[14].

Presence of co-morbidity like diabetes did not delay sputum conversion rate in the present study and also in other studies[16].Addiction to tobacco or other drugs

also did not have an influence or association with smear conversion and same was reported by other worker[16].

Tuberculosis remains a major disease in the third world countries and its successful treatment is very important for the complete eradication of the disease. Factors like hemoglobin levels, ESR, initial bacillary load, gender and duration of symptoms must be monitored as important indicators along with microbiological parameters to ensure successful treatment of tuberculosis.

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Authors Contribution

AAS and SR collected and interpreted the data as well as wrote the manuscript. MKM supported in designing and supervising the study. RI supported in designing, supervising and writing the manuscript. MA did the statistical analysis. SS supported in writing manuscript.

Conflict of interest: None declared.

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