

Factors Influencing Sputum Smear and Culture Conversion Time among Patients with Pulmonary Tuberculosis

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ABSTRACT

Introduction: Pulmonary tuberculosis is a contagious bacterial infection that involves the lungs and it may spread to other organs. Sputum smear and culture conversion are important indicators for the effectiveness of treatment and the infectivity of the patient. The present study aims to find sputum smear and culture conversion time and the factors that influence the conversion time among tuberculosis patients at National Tuberculosis Centre in Nepal.

Methods: A total of 54 patients, who were diagnosed with laboratory confirmed pulmonary tuberculosis and under antitubercular therapy were monitored for sputum smear and culture conversion time. The blood specimens from each patient were processed for hemoglobin, platelets, erythrocyte sedimentation rate and blood glucose levels. Patient's clinical history, risk factors that prolong conversion time and sociodemographic information were also collected by direct interview.

Results: The mean sputum smear and culture conversion were found to be 54.4 days and 45.5 days respectively. Old age, smoking habit, low body mass index value, Treatment category II, initial bacillary load and abnormal erythrocyte sedimentation rate values were found to be associated with long sputum conversion time. Radiographic involvement of only left lungs, presence of fewer symptoms, aged between 15-45 years, having normal weight, without smoking habit and being married, were found to be associated with short sputum conversion time.

Conclusions: The sputum microscopy, old age, smoking habit, low body mass index value, treatment category II, initial bacillary load and abnormal erythrocyte sedimentation rate value had been found to be significantly associated with long sputum conversion time.

Keywords: culture conversion time; factors influencing conversion time; pulmonary tuberculosis; sputum smear.

INTRODUCTION

Tuberculosis (TB) is caused by tubercle bacilli i.e. *Mycobacterium tuberculosis* and occasionally by *M. bovis* and *M. africanum*. Ten to fifteen peoples are estimated to be infected by each untreated cases, which makes Tuberculosis, a disease of public health importance worldwide with significant morbidity and mortality.¹

There is an annual rise of 21,827 smear positive infectious tuberculosis incident cases in the country.² The introduction of Directly Observed Treatment Short-course (DOTS) has dramatically reduced the numbers of deaths from 9712 (51/100) in 1990 to 6436 (23/100) in 2007.

Although the expansion of DOTS has proved its efficacy in Nepal, the treatment success rate is not 100%; it reached 89% in 2008.² The relapse of tuberculosis continues to place a substantial burden on patients and tuberculosis control programs.³

Monitoring of tuberculosis patients during treatment is significant in order to establish patient's treatment outcomes and to measure the national program effectiveness.⁴

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This study aimed to evaluate risk factors such as age, initial smear grade, body mass index (BMI), hematological and radiological manifestations, diabetes mellitus, etc. which are likely to influence smear and culture conversion.⁵

METHODS

The study was conducted at National Tuberculosis Centre (NTC) and South Asian Association for Regional Co-operation Tuberculosis Centre and HIV/AIDS Centre (STAC), Thimi, Bhaktapur. During the study period, 13,557 patients visited the hospital. Among them 2778 patients were diagnosed for tuberculosis. Among these patients, Extensively Drug-Resistant (XDR) and Multidrug-Resistant (MDR) TB patients, extra pulmonary, pulmonary tuberculosis (PTB) patients with negative smear, patients from out of valley who were not able to have monthly visit and patients who were not interested to be the part of the study were excluded from the study. A total of 145 confirmed PTB based on sputum microscopy and chest X-ray and under antitubercular therapy were further monitored for sputum smear and culture conversion. Among these only 54 patients were in regular monthly follow up and included in this study.

After the patient was diagnosed as a PTB patient by hospital, counseling was provided on the same day about the research, and written consent as well as research questionnaire were taken from each study participant. Sputum specimens were collected in leak proof, wide mouth, transparent, sterile and stopper plastic container with proper verbal instruction for the quality sputum specimen. For hematological examination and estimation of blood glucose, about 5 ml of blood specimens were collected through vein puncture.⁶⁻⁸

The collected specimens were stained by Ziehl-Neelsen method and processed for culture.^{9,10}

The culture of sputum specimens was continued monthly after antitubercular therapy to find out culture conversion time. Sputum specimens were concentrated and decontaminated by modified petroff method¹¹. Identification of significant isolates were done by using standard microbiological

techniques as described in Bergey's Manual of Systemic Bacteriology (2004).

The patients after the diagnosis as PTB were subjected to antitubercular therapy. For new sputum smear-positive PTB patients were kept in treatment category I and for relapse, treatment failure, treatment after default (interrupted treatment) patients were kept in treatment category II and referred to their nearby DOTS center.

The patients included in the research were monitored monthly for sputum till the smear and culture conversion. During follow up, sputum specimens were collected monthly and examined by microscopy and culture.

RESULTS

Only 54 patients with laboratories confirmed PTB were regular in monthly follow-up with submission of sputum specimen till sputum smear and culture conversion. Table below summarizes the background characteristics of recruited patients. It also demonstrates the possible factors for long sputum smear and culture conversion time and the relation of the factors with sputum smear and culture conversion time. The mean sputum smear conversion was found to be 54.4 days, whereas mean sputum culture conversion was found to be 45.5 days. The factors that prolong sputum conversion time were old age, smoking habit, under weight or low BMI, relapse or treatment failure or treatment after default cases with treatment category II, initial high bacillary load (3+) and abnormal ESR value. They had been found to be associated with long sputum conversion time with sputum smear conversion of 56 to 68.2 days and sputum culture conversion time of 47 days to 57.7 days. The factors influencing short conversion time were radiographic involvement of only left lung, presence of less number of symptoms (two or less), aged between 15-45 years, normal ESR value having normal weight, and without smoking habit. They had been significantly correlated with short sputum conversion time with sputum smear conversion of 41.7 to 56.5 days and sputum culture conversion time of 31.9 days to 47.8 days. The factors without any influence in sputum smear and culture conversion time were found to be occupation of the patients, hemoglobin concentration,

random blood glucose level and platelet count.

All 54 Tuberculosis patients were interviewed personally through the questionnaire.

Table 1. Characteristics of TB patients and relation with sputum conversion.

Factors	Patient included n (%)	Mean conversion time (days)	
		Smear	Culture
Age a. ≤15	1 (1.8)	60	60
b. 15-45	39 (72.2)	51.5	46.1
c. ≥ 45	14 (26)	57.8	57.8
Gender a. Female	20 (37.0)	57	43.5
b. Male	34 (63.0)	52.9	51.1
Marital status a. Unmarried	16 (29.6)	58.2	49.4
b. Married	38 (70.4)	52.7	47.8
Occupation a. Risk level I	17 (31.5)	58.2	45.9
b. Risk level II	17 (31.5)	54.7	47.6
c. Risk level III	20 (37.0)	48	51
Weight (BMI) a. Under Wt(<19)	31 (57.4)	68.2	57.1
b. Normal Wt(20-25)	23 (42.6)	41.7	31.9
Smoking habit a. No Smoking	37 (68.5)	53.5	47.8
b. Smoking	17 (31.5)	56.5	56.5
Symptoms a. Two or less	12 (22.2)	52.5	47.5
b. Three	20 (37.0)	55.5	49.5
c. Four or more	22 (40.7)	54.5	47.7
Case a. New case	43 (79.6)	53	46
b. Relapse/treatment failure/default	11 (20.4)	60	57.3
Initial smear grade a. 1+	24(44.4)	49	50
b. 2+	16(29.6)	54	47
c. 3+	14(25.9)	68	47
Cavity a. Right lungs	12 (22.2)	57.5	55
b. Left lungs	12 (22.2)	45	47.5
c. Both lungs	30 (77.8)	57	46
Hemoglobin a. Minimum level	33 (61.1)	53.6	46.4
b. Normal level	20 (37.0)	49.5	57
c. Maximum level	1 (1.9)	30	60
Blood glucose a. Minimum level	1 (1.85)	30	30
b. Normal level	39 (72.2)	55.7	50.8
c. Maximum level	4 (7.4)	30	37.5
ESR a. Abnormal value	45 (83.3)	56	48.6
b. Normal value	9 (16.7)	46.6	46.6
Platelet Count a. Normal	40 (74.1)	63	54.7
b. Thrombocytosis	14 (25.9)	30	30
Mean	54	54.4	45.5

DISCUSSION

In this study, most of the patients had the sputum conversion time in the range of one to two months. The mean sputum smear conversion was found to be 54.4 days, whereas mean sputum culture conversion was found to be 45.5 days, shorter than sputum smear conversion. The study in Tanzania had found the mean sputum smear conversion time of 59.4 ± 32.2 days and mean culture conversion time of 57.1 ± 29.9 days.¹² As at the end of two months, microscopy may also show non-viable bacilli, which are either dead bacilli or bacilli unable to reproduce; which may be the reason for the difference in percentage and mean conversion time of smear and culture conversion time.¹²

The mean sputum smear and culture conversion time in the elderly patients with the age more than 45 was found 57.8 days which was comparatively longer than that in the patients between the age 15 and 45. The percentage of the patients with one-month sputum conversion time is similar with the age group 15-45 and ≥ 45 , which is between 40-50%. The mean sputum smear and sputum culture conversion in the patients with age group 15-45 had been found 51.5 days and 46.1 days, which is a significant difference within the different age groups. The poor immune system in elderly people may be the cause of the long conversion time in compare to patients with age group between 15-45. The study of sputum conversion time in the age group ≤ 15 had not been significant due to minimum percentage of the specimen group. In the study, it was found only 36% of elderly above age 65 people have culture conversion, 63.7% of elderly of age 45-64 have sputum conversion and 64.6% of patients of age 25-44 had sputum conversion at the end of two months of intensive phase of treatment. The study in Tanzania had also found the similar relation between the old age and delayed sputum conversion time.¹³

In this study, the relation between the gender and conversion time had been found to be contradictory. The percentage of the male patients is more in both short conversion time and long conversion time in comparison to the female patients. The mean sputum smear and culture conversion had been found to be 52.9 days and 51.1 days in male and 57

days and 43.5 days in female respectively. The contradictory result may be due to maximum variation in the personal status of male patients like smoking habit, alcoholism, occupation and immune status, which was found to be more consistent in the female patients.^{5,14}

BMI of patient indicates the height weight suitability. The mean sputum smear and culture conversion time in under-weight patients was 68.2 and 57.1 days respectively which is comparatively less in normal weight patients i.e. 41.7 and 31.9 days. We found that 68.1% and 59.1% of patients with normal weight (BMI value between 20-25 kg/m²) had one month smear and culture conversion time respectively, where as only 21.9% and 40.6% of the patients with under weight (BMI < 19) have one month smear and culture conversion time respectively, which is the significant relation. In the earlier study in Mwanza, the patients with a BMI value less were more likely to remain sputum culture positive than those with a normal BMI value, although the results were not significant.¹⁴

Furthermore, although the difference in the mean sputum smear and conversion time is less in smokers and non-smokers, the significant difference was observed only in sputum culture conversion time which is 47.8 days in non smokers and 56.5 days in smokers. The risk of smoking in TB patients had been stated by WHO that smoking influences the clinical progress of TB lesions. Smokers tend to have more cavitory disease, and greater severity despite diagnostic delays similar to those among non-smokers. Similar result was found in Tanzania that there is relation between smoking habit and delayed sputum smear conversion.¹⁴ A similar study in Spain concluded that the smoking habits delay sputum conversion in patients with pulmonary tuberculosis not associated with HIV and non-resistant bacilli.¹⁵

During the comparison of the new case patients receiving treatment category I and relapsed/treatment failure/treatment default receiving treatment category II with sputum conversion, significant difference had been observed with both sputum smear and sputum culture conversion time. Comparatively the new case patients receiving treatment of category I had short

sputum smear and culture conversion time, i.e. 53 and 46 days respectively, which were 60 and 57.3 days respectively in case of patients receiving category II. In close observation, the significant difference had been observed in the case of long sputum conversion time.

Another risk factor, initial bacillary load on the sputum smear conversion has also been reported by the similar study in Gambia and Thailand.^{16,17} The study in Thailand found the sputum smear conversion at the end of two months as 90.9%, 77.9%, 61.7% among patients with initial weak, moderate and strong positivity respectively.¹⁷ The study in Gambia observed that treatment failure was associated with increasing bacillary load.¹⁶ The study in Tanzania had found sputum smear conversion time of 48.24 ± 28.66 days, 60.11 ± 34.28 days, and 71.66 ± 30.6 days in the patients with initial smear grade or bacillary load of 1+, 2+ and 3+ respectively. In case of sputum culture conversion, time was 46.61 ± 25.43 days, 60.22 ± 35.27 days, and 67.46 ± 28.8 days in the patients with initial smear grade or bacillary load of 1+, 2+ and 3+ respectively.¹² In this study the mean sputum smear conversion was found to be similar to the above for sputum smear conversion, in case of sputum culture conversion the result is contrary and not found to be significant.

Moreover, no relation had been found between bilateral radiographic involvement and sputum conversion, whereas in contrary the relation had been found between involvement of left lung and short sputum conversion time. Factor bilateral radiographic involvement had been found to be associated with lack of smear conversion in the similar study in Chennai, India.¹²

In addition, no relation had been found between low concentration of hemoglobin and long sputum conversion time. In this study, we had not found any relation between blood sugar level and long sputum conversion time. The result is contrary to the previous study. The deviation might be due to minimum percentage of patients with maximum blood glucose level in the blood. In similar study in Indonesia suggested that diabetes is very strong risk factor for TB.¹⁸

The present study found strong relation between the abnormal value of ESR and long

sputum conversion time. The mean sputum smear conversion of the patients with abnormal value of ESR had been found to be comparatively long. Although the sputum culture conversion was long in patients with abnormal ESR value, the difference is not significant. All the patients with long sputum conversion (three and four months) were found to have abnormal ESR value. However, in the similar study in Tanzania et al., 2006 did not found statistically significant correlation between the sputum conversion and ESR value.^{12,18}

CONCLUSIONS

The monthly monitoring of the PTB patients for sputum conversion is the most important indicator for the effectiveness of treatment and the infectivity of the disease. The significant resemblance had been found in the results obtained from the sputum microscopy and sputum culture, however, the mean sputum smear conversion time had been found slightly higher than mean sputum culture conversion time. Old Age, smoking habit, low BMI, treatment category II, initial bacillary load and abnormal ESR value had been found to be significantly associated with long sputum conversion time.

Radiographic involvement of only left lung, presence of less number of symptoms (two or less), aged between 15-45 years, having normal weight, without smoking habit and being married, had been found to be significantly associated with short sputum conversion time.

However, the concentration of hemoglobin, thrombocytosis, bilaterally radiographic involvement and presence of maximum number of symptoms had not been found associated with long sputum conversion.

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