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ORIGINAL RESEARCH

Cough Frequency and Outcome among pulmonary TB patients of a Private tertiary care hospital Indore, Madhya Pradesh

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ABSTRACT

Introduction: Patients with pulmonary TB present with a chronic productive cough, fever, and weight loss. Cough occurs in a variety of circumstances, notably in acute upper and lower respiratory infections. However, these acute infections often resolve within weeks. Cough in people with pulmonary TB disease arises as a result of the inflammatory response to mycobacterium pulmonary infection.

Objectives: to assess the change of cough frequency and pulmonary T.B outcome.

Method: observational study conducted in tertiary care hospital among all 250 in and out patients of pulmonary T.B. Data were entered first into Excel and then analyzed using STATA version 11.0 for Windows.

Results: The study shows statistically significant association between 7 an 14 days and 14 and 30 days cough frequency improvement. The study shows as the cough frequency is improving (decrease in 24 hour), outcome is also going to be good at 7 and 14 days with a statistically significant P-value of 0.000.

Conclusion: Thus, cough frequency during the first two weeks of therapy should be used as part of the routine clinical evaluation. Patients with unchanged or increased cough frequencies after two weeks of treatment should be more closely followed as they are at risk of adverse outcomes.

INTRODUCTION

The Mycobacterium tuberculosis complex includes five species: *M. tuberculosis, M. bovis, M. canetti, M. africanum, and M. microti*. Most human disease is caused by *M. tuberculosis*. These bacilli, transmitted on airborne droplets, can cause a lung disease that if left untreated will kill about 50% of patients.[1]95% of cases and deaths occur in developing countries and

TB accounts for approximately 70% of all deaths in developingcountries.[2]Globally, TB is currently responsible for more years of healthy life lost (2.5 percent of all disability-adjusted life years, or DALYs) than any other infectious disease, bar AIDS and malaria[3] Further exacerbating the global TB problem is the continuing emergence of multidrug resistant (MDR) TB. MDR-TB is resistant to treatment with isoniazid and rifampicin—the two most potent first-line TB drugs. Diagnosis and treatment of MDR-TB in endemic areas is a relatively new public health challenge.

Despite the successes achieved by the adoption of the Directly Observed Therapy, short course (DOTS) strategy in countries such as INDIA, the recent emergence of multidrug resistant (MDR) TB and extremely drug resistant (XDR) TB has slowed down the progress toward the ultimate goal of TB control and elimination.

Patients with pulmonary TB present with a chronic productive cough, fever, and weight loss. Cough occurs in a variety of circumstances, notably in acute upper and lower respiratory infections. However, these acute infections often resolve within weeks. Cough in people with pulmonary TB disease arises as a result of the inflammatory response to mycobacterium pulmonary infection. A reduction in cough is assumed to represent adequate response to treatment, and to result in decreased risk of spread of infection.[4]thus, a patient with a cough for longer than two weeks, especially after a course of antibiotics, should be investigated for pulmonary TB.

Very few studies have been done in the past to assess cough frequency and outcome of pulmonary T.B. This study will definitely add to fight against T.B .The importance of a study will have more in developing countries like India with limited resources and manpower. This study will be more useful for identifying early case detection without spending much money, though furthermore studies and data need to be required.

The purpose of undertaking this study was to explore the use of cough frequency as a clinical marker for treatment efficacy. Understanding this correlation promises to deliver an inexpensive and reliable method of determining treatment efficacy, especially in the era of MDR TB and XDR TB.

OBJECTIVES

1. To assess the change of cough frequencies and pulmonary TB patients out come over time.

METHODOLOGY

TYPE OF STUDY

Prospective Observational Study.

STUDY PLACE

Tertiary care hospital of Madhya Pradesh

STUDY PERIOD

June 2017-June 2018

STUDY POPULATION

Patients under the care of the Index Medical College, Hospital &Research centre, Indore, on both inpatient and outpatient .Patients with TB suspected either clinically or radiologically are recruited for the study.

INCLUSION CRITERIA

- 18 years of age or older.

- Active pulmonary tuberculosis diagnosed by positive sputum smear and/or sputum culture.

EXCLUSION CRITERIA

- Pregnant at time of subject screening.
- Unwilling or unable to provide informed consent.
- Presence of extra-pulmonary tuberculosis
- HIV Positive

STUDY SAMPLE

A total of 250 patients started anti-TB treatment during the period of study and were eligible for this study. However, 43 patients lost to follow up, and 7 died irrespective of TB. Therefore, only 200(80%) patients were included in the analysis

DATA COLLECTION

Prior to initiation of data collection informed consent have been taken. In this study, a semi-structured with open ended questionnaire have been used tointerview. A total 250 study participants have answered, who diagnosed with pulmonary tuberculosis.

Patients chose to provide their informed consent; they underwent a chest x-ray (CXR), a review of the history and a physical exam. Once these exams were completed, patients were hospitalized in the Index Medical College, Hospital &Research centre for a period of between 7 and 14 days. Day 0 is defined as the day that a new anti-TB regimen was started, whether primary treatment or retreatment.

The main variable of the study was cough frequency, recorded in the questionnaire as coughs per day on days -0 (start of treatment) 7, 14,30, and 60 (days). During the study the following data were collected: patient weight, self-reported cough frequency and self-reported medication compliance. At day 14, patients were discharged if appropriate for their clinical condition, and subsequently followed as outpatients.

If the patients' health permitted, and they so desired, they were sometimes discharged as early as day 7 and subsequently followed as outpatients. When patients returned for outpatient appointments, the same information was obtained. The study terminated at day 60.

The patients were dichotomized by those having a good outcome (sputum negative at the end of 60 days) and those having an adverse or poor outcome (sputum positive at the end of 60 days). Other variables of interest included in the analysis were: age measured in years, patient sex (male or female).

DATA ANALYSIS

Data were entered first into Excel and then analyzed using STATA version 11.0 for Windows. Appropriate analysis was carried out to evaluate cough frequency over time. T test and setting a two-sided alpha to .05 and confidence interval 95% to compare subjects with improved cough frequency to subjects with not improved cough frequency. P value <0.05 is considered significant.

OBSERVATIONS AND RESULTS

In our study there were total 147 (73.5%) male and 53 (26.5%) female have participated with the mean age was 44.99 years (range: 18-55).

Table shows the associations found between cough frequencies improvement at different time intervals. The study shows statistically significant association between 7 an 14 days and 14 and 30 days cough frequency. But the association between cough frequency improvement of 30 and 60 days was not found statistically significant**.** (Table 1)

Table 1: Association of cough frequencies at different time intervals

Cough Frequency improved at 7 Days	**Cough Frequency improved at 14 days**		**Total**
	Improved	**Not Improved**	
Improved	171(93.44)	7(41.18)	178 (89.00)
Not Improved	12(6.56)	10(58.82)	22(11.00)
Total	183(100)	17(100)	200(100.00)
Pearson chi-square 43.404 ,DF -1,P-value- 0.000			
Cough Frequency improved at 14 days	**Cough Frequency improved at 30 days**		
	Improved	Not Improved	
Improved	178(94.59)	8 (53.33)	183(91.50)
Not Improved	10 (5.41)	7 (46.67)	17 (8.50)
Total	185 (100.0)	15 (100.0)	200(100.00)
Pearson chi-square 30.372 ,DF -1,P-value- 0.000			
Cough Frequency improved at 30 days	**Cough Frequency improved at 60 days**		
	Improved	Not Improved	
Improved	115 (93.50)	70 (90.91)	185 (92.50)
Not Improved	8 (6.50)	7 (9.09)	15 (7.50)
Total	123 (100.0)	77 (100.0)	200 (100.0)
Pearson chi-square 0.457 ,DF -1,P-value- 0.499			

Table shows the association between cough frequency and outcome at 7 days. The study shows as the cough frequency is improving (decrease in 24 hour), outcome is also going to be good at 7 days with a statistically significant P-value of 0.000.

Table shows the association between cough frequency and outcome at 14 days. The study shows as the cough frequency is improving (decrease in 24 hour), outcome is also going to be good with a statistically significant P-value of 0.000.

Table shows the association between cough frequency and outcome at 30 days. The study shows as the cough frequency is improving (decrease in 24 hour), outcome is also going to be good with a statistically significant P-value of 0.000.

Table shows the association between cough frequency and outcome at 60 days. The study shows as the cough frequency is improving (decrease in 24 hour), outcome is also going to be good with a statistically significant P-value of 0.019. (Table no. 2)

Table 2: Association between cough frequency and outcome at different time intervals (7 days, 14 days, 30 days and 60 days)

Cough Frequency improved at 7 Days	**Outcome**		**Total**
	Good	**poor**	
Improved	173 (97.74)	5 (21.74)	178 (89.00)
Not Improved	4 (2.26)	18 (78.26)	22(11.00)
Total	177(100)	23(100)	200(100.00)
Pearson chi-square 120.096, DF -1, P-value- 0.000			
Cough Frequency improved at 14 days	**Out Come**		
	Good	Poor	
Improved	174 (98.31)	9 (39.13)	183(91.50)
Not Improved	3(1.69)	14 (60.87)	17 (8.50)
Total	177 (100.0)	23 (100.0)	200(100.00)
Pearson chi-square 91.644, DF -1, P-value- 0.000			
Cough Frequency improved at 30 days	**Out Come**		
	Good	Poor	

Improved	177 (100)	8 (34.78)	185 (9.50)
Not Improved	0 (0.00)	15 (65.22)	15 (7.50)
Total	177 (100.0)	23 (100.0)	200 (100.0)
Pearson chi-square 124.794, DF -1, P-value- 0.000			
Cough Frequency improved at 60 days	**Out Come**		
	Good	Poor	
Improved	114(64.41)	9(39.13)	123(61.50)
Not Improved	63(35.59)	14(60.87)	77(38.50)
Total	177(100)	23(100)	200(100)
Pearson chi-square 5.492, DF -1, P-value- 0.000			

DISCUSSION

This study shows that, after adjusting for potential confounders, cough frequency over time among patients who developed adverse outcomes is completely different from patients classified in the good outcome group at the end of the study. The association continues being statistically significant after having included the monthly sputum microscopy result as confounder, pointing out that change in cough frequency over time is an independent predictor of treatment outcome.

These findings might have an important impact on public health, especially in resource limited settings. Cough frequency assessment might be an easy, cheap, and useful way to predict anti-TB treatment outcome among pulmonary TB patients receiving therapy. Constant or increased cough frequency after the end of the first two weeks of therapy might be an important indicator that further attention is needed to help avoid deaths or failures. Remarkably, most of the divergence of cough frequency over time occurred during the first two weeks of anti-TB therapy. After that, cough frequency among poor outcome patients shows parallel trends compared to good outcome ones with, however, a slightly lower rate.

The first and only study carried out by ***Loudon et al.***[5]that looked specifically at cough frequency as an index of infectivity and to measure changes in cough frequency in TB patients during treatment with anti-TB antibiotics. Study found that cough frequency at the time of admission did not prove to be a satisfactory index of infectivity, the decline in cough frequency during treatment with anti-TB drugs was rapid. Most patients reduced their cough count to half the initial value within two weeks. Thus, patient's cough frequency might be a helpful and inexpensive marker to predict TB treatment outcome.

Jesus Gutierrez et al conducted a study on[1] Correlation of Cough Frequency with Treatment Efficacy in Pulmonary Tuberculosis Patients in Lima, Peru. Out of total 250 eligible patiemt141 (56.4%) patients were included in the analysis. 13 (9.2%) had a poor outcome at the end of the study period (11 had failed and 2 died). Study shows detailed description of cough frequency variation during treatment follow-up without accounting for intra-subject correlation. There was no significant difference between cough frequency of the outcome groups at baseline (p = 0.12). However, on average, during the first two weeks cough frequency did not decrease in those who developed an adverse outcome whereas it declined among those who had a good outcome.

Friedland JS, Proano A **et *al.*** [6]done study Cough Frequency during treatment Associated with Baseline cavitary Volume and Proximity to the Airway in Pulmonary TB

Study found that Cough frequency during treatment was twofold higher in participants with large cavity volumes (rate ratio [RR], 1.98; P ¼ .01) and cavities located closer to the airway (RR, 2.44; P ¼ .001). Comparably, cough ceased three times faster in participants with smaller cavities (adjusted hazard ratio [HR], 2.89; P ¼ .06) and those farther from the airway (adjusted HR, 3.61;, P ¼ .02). Similar results were found for bacillary burden and culture

conversion during treatment. Above study also gives supportive result to our study to predict out come from Cough frequency.

CONCLUSION

The findings of this study reveal that trends and change of cough frequency during anti-TB therapy can predict treatment outcome. Thus, cough frequency during the first two weeks of therapy should be used as part of the routine clinical evaluation.

STUDY LIMITATION

Other co-morbidities which can present or include cough in their symptomatology could not be excluded. Finally, the determination of cough frequency was done through the administration of a questionnaire. As with all studies based on this data-gathering method, it was subject to recall bias by the patients. it is possible that those patients who were sicker or had a higher rate of coughing remembered more accurately than those who had a lower or decreasing cough frequency. Another important bias associated with the administration of the questionnaire is the response bias.

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Nil

CONFLICT OF INTEREST

None

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