

Role of Sputum Smear in Predicting Culture Results in Pulmonary Tuberculosis

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ABSTRACT

Aim: To determine the role of sputum smear in predicting the culture results in pulmonary tuberculosis.

Study Design: Cross sectional study

Place and duration: Rashid Latif Medical College and CMH, Lahore from Jan 2009 to Dec 2012

Methods: A total of 200 patients with positive sputum smear and sputum culture were selected by non probability convenient sampling but 20 patients lost to follow up and excluded from study. All the patients were given standard 04 drugs anti tuberculosis treatment in the intensive phase and Isoniazid (INH), Rifampicin and Myambutol in continuation phase. Sputum smear examination and culture was performed in every patient at end of second month of treatment.

Results: Out of 180 patients 129(71.7%) were male and 51(28.3%) were females. At two months 108(60%) patients were Sputum smear negative and 72(40%) were smear positive. Out of 108 smear negative patients 93(86.1%) were culture negative and 15(13.9%) were culture positive ($p<0.005$). Out of smear positive patients 48(66.7%) were culture positive and 24(33.3%) were culture negative ($p<0.005$). Sensitivity and specificity of 02 months sputum smear in predicting the culture conversion is 76.19% and 79.49% respectively.

Conclusion: The sensitivity, specificity, positive predictive value and negative predictive value of sputum smear examination in predicting the sputum culture result, are quite low. Sputum smear examination cannot be used as a substitute for sputum culture conversion at two months. However a negative sputum smear at two months is a strong predictor of culture negativity.

Keywords: Tuberculosis, smear conversion, culture conversion

INTRODUCTION

Pulmonary tuberculosis control involves the effective treatment and adequate measures to limit spread of infection. The most important is the achievement of treatment response as early as possible. Response to treatment in pulmonary TB patients is monitored by sputum smear examination and sputum culture. In the controlled trials using various drugs combinations the sputum culture conversion is used as surrogate marker of long term cure and predictor of relapse¹⁻³. The efficacy of different regimen is tested by using this parameter. The culture of mycobacterium tuberculosis is time consuming and expensive. The facilities for culture are not available in most of the countries with high burden of tuberculosis especially the developing countries. An alternative to culture conversion testing is the smear conversion that is commonly used to assess the infectivity of patient, response to treatment and to document the cure of tuberculosis. It is easily performed, available in most

of the laboratories and very cost effective. The disadvantage is, not all smear positive patients are culture positive and not all smear negative patients are culture negative⁴⁻⁶. Studies have demonstrated the role of sputum smear in predicting the outcome of tuberculosis but the predictive role of sputum smear is less consistent than the predictive role of sputum culture. This relationship of sputum smear and sputum culture has not been studied well in the past. Very few studies are available that quantify the relation of sputum smear and sputum culture in terms of sensitivity, specificity and predictive value. The results are not consistent and some studies undervalue the role of sputum smear and others over rate its significance⁷. Quantification of role of sputum smear in predicting the culture conversion is of paramount importance. Once we are able to make out the predictive value of this relationship we can use the less expensive, readily available and easier to perform sputum smear examination instead of sputum culture for monitoring treatment response, treatment failure, infectivity and relapse in tuberculosis patients. In order to reinforce the existing data available on this subject we designed a study to find out the sensitivity, specificity and predictive value of sputum smear in predicting the result of sputum culture.

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MATERIAL AND METHODS

This cross sectional study was conducted in the Rashid Latif Medical College and CMH, Lahore from Jan 2009 to Dec 2012. Patients presenting with symptoms suggestive of tuberculosis were screened by detailed history, physical examination, X-ray chest, blood complete picture, erythrocyte sedimentation rate (ESR), sputum smear examination and sputum culture. A total of 200 patients with positive sputum smear and sputum culture were selected by non probability convenient sampling. Patients who had smear negative, culture negative, previously treated for tuberculosis, primary drug resistance, uncontrolled diabetes mellitus, renal failure, hepatic failure, Human Immunodeficiency Virus infection and pregnancy were excluded from the study. All the patients were given standard 04 drugs anti tuberculosis treatment in the intensive phase and Isoniazid (INH), Rifampicin and Myambutol in continuation phase. All the patients were managed as outdoor patients and directly observed therapy (DOT) was not practiced. Sputum smear examination and cultures were performed in every patient at end of second month of treatment. BACTEC was used for culture. The data was collected on data collection form and SPSS 18 was used for statistical analysis. The sensitivity, specificity, positive predictive and negative predictive value of sputum smear was calculated. Chi square was used to compare proportions and T test was used to compare means. P value <0.05 was considered significant.

RESULTS

A total of 200 patients were included in the study but 20 patients lost to follow up and excluded from study. Out of remaining 180 patients 129(71.7%) were male and 51(28.3%) were females. At two months 108(60%) patients were Sputum smear negative and 72(40%) were smear positive. Out of 108 smear negative patients 93(86.1%) were culture negative and 15(13.9%) were culture positive ($p < 0.005$). Out of 72 smear positive patients 48(66.7%) were culture positive and 24(33.3%) were culture negative ($p < 0.005$). The sensitivity specificity, positive predictive value and negative predictive value of sputum smear in predicting the culture results are shown in table 1. Treatment failure was observed in 33(18.4%). None of the patients in 02 month smear negative group was treatment failure. In the treatment failure group culture reports revealed 24 (sensitive to first line drugs), 3 (resistant to INH), 3 (resistant to drugs other than INH and Rifampicin) and 3 (MDR cases).

Table 1: Predictive value of sputum smear in predicting culture results

Sensitivity	76.19%	95% CI: 63.79%- 86.01%
Specificity	79.49%	95% CI: 71.03% to 86.39%
+ve predictive value	66.67%	95% CI: 54.57% to 77.34%
-ve predictive value	86.11%	95% CI: 78.13%- 92.01 %

DISCUSSION

In our study the rate of sputum smear conversion is 60%, the sputum culture conversion rate is 86.1% in smear negative, 33.3% in smear positive and over all culture conversion rate is 65%. Rate of sputum smear and culture conversion at two month has been reported to vary from 50.4% to 98.6% in various studies. In 2012 Viser et al. conducted a study in south Africa on sputum smear and culture positive tuberculosis patients and reported a 02 month culture conversion rate of 50.4% but 89% of his patients were having cavitatory tuberculosis and this factor alone strongly affects the culture conversion rate at two months⁸. Tiwari et al. conducted a study on smear positive tuberculosis in India and reported smear conversion rate of 57.9% among the High Positive smear and 71.6% in the Low positive smear patients. In this study the DOT was carried out and in our study we did not follow the DOT. The DOT therapy improves compliance and is a powerful factor that affect the outcome and culture conversion rate⁹. Banu et al. in 2007 studied the smear conversion and culture conversion in non diabetic, diabetic and HIV positive cases. He reported the smear conversion of (58, 61, and 62%) and culture conversion (86, 88 and 92%) in pulmonary tuberculosis alone, tuberculosis in type II diabetes and tuberculosis in HIV positive respectively. The study concluded that the sputum smear or culture conversion was dependent on age more than 45 years, higher pretreatment smear and extent of the disease¹⁰. The results of this study are consistent with our study. Felix et al. in 2013 reported a smear conversion rate of 80% and he concluded that initial higher smear grade ,HIV infection and non adherence to treatment was associated with non conversion¹¹. In 2012 Caetano et al, observed a smear conversion rate of 74.6% and culture conversion rate of 72.8%. Age \geq 50 years , male gender and higher smear grade were significantly associated with persistent smear positivity after 2 months of treatment and bilateral radiological involvement was associated with persistent culture positivity¹². Rieder in 1996 reported 75% culture conversion rate, with a range from 61.7% to 90.9% in patients with initially strongly- and weakly-positive smears, respectively. He concluded that smear positivity at two months strongly predicted the culture results¹³. Bawri et al. in 2008 reported 84% smear conversion rate, slightly higher rate of smear conversion than our study but in this study the short

course DOTS regimen was used and DOTS is known factor to improve the compliance and ultimately the outcome in pulmonary tuberculosis¹⁴. Khalid in 2013 reported a 95% sputum smear conversion in his study but the study did not compare the culture results¹⁵. Mbazi et al in 2010 observed 98.6% and 97.0% 2 month sputum conversion rate and culture conversion rate of 98.6% and 97% in HIV positive and HIV negative patients respectively¹⁶. The high success rate of smear and culture conversion in this study could be attributed to DOTS. Factors that affect sputum smear conversion include old age, male sex, smoking, thrombocytosis, sputum collection techniques, base line smear grade extent of disease, drug compliance and drug resistance. The presence of diabetes mellitus, extensive or cavitary disease, high pretreatment smear grade and a past history of tuberculosis are factors influencing both sputum smear and culture conversion time in pulmonary TB^{17,18}.

Our study has shown that sensitivity and specificity of 02 months sputum smear in predicting the culture conversion is 76.19% and 79.49%, respectively. Positive and negative predictive value of sputum smear is 66.67% and 86.11%, respectively. The sensitivity, specificity and positive predictive value are quite low however the negative predictive value of sputum smear is quite reasonable but not significantly high. Atypical mycobacterium, inefficient laboratory techniques commonly yield false positive smears⁶. The results of our study are consistent with other studies. In 2007 a study conducted by Su W, revealed that the sensitivity and specificity of 2-month sputum smears in predicting 2-month culture conversion were 64.3% and 81.6%, respectively³. In our study we could not implement DOT and poor compliance may be the reason of 24(33.3%) treatment failures despite the fact that isolate was sensitive to all first line drugs.

CONCLUSION

The sensitivity, specificity, positive predictive value and negative predictive value of sputum smear examination in predicting the sputum culture result, are quite low. Sputum smear examination cannot be used as a substitute for sputum culture conversion at two months.

REFERENCES

1. Wallis R, Johnson J. The role of surrogate markers in the clinical evaluation of antituberculous chemotherapy. *Current Medicinal Chemistry-Anti-Infective Agents* 2005;4(4):287-94.
2. Sajid MD, Imran M, Siddique M. Addition of amikacin and levofloxacin is associated with higher culture conversion rate in pulmonary tuberculosis. *PJMHS*. 2011;5(3):450-4.

3. Su W, Feng J, Chiu Y, Huang S, Lee Y. Role of 2-month sputum smears in predicting culture conversion in pulmonary tuberculosis. *European Respiratory Journal*. 2011;37(2):376.
4. Horne DJ, Johnson CO, Oren E, Spitters C, Narita M. How soon can smear positive tb patients be released from inpatient isolation? *Infection control and hospital epidemiology: the official journal of the Society of Hospital Epidemiologists of America*. 2010;31(1):78.
5. Ramarokoto H, Randriamiharisoa H, Rakotoarisaonina A, Rasolovavalona T, Rasolofo V, Chanteau S, et al. Bacteriological follow-up of tuberculosis treatment: A comparative study of smear microscopy and culture results at the second month of treatment. *The International Journal of Tuberculosis and Lung Disease*. 2002;6(10):909-12.
6. Lee JS, Kim E-C, Joo SI et al. The incidence and clinical implication of sputum with positive acid-fast bacilli smear but negative in mycobacterial culture in a tertiary referral hospital in south korea. *J Korean Med Sci*. 2008; 23(5): 767-71.
7. Horne DJ, Royce SE, Gooze L, Narita M, Hopewell PC, Nahid P, et al. Sputum monitoring during tuberculosis treatment for predicting outcome: Systematic review and meta-analysis. *The Lancet Infectious Diseases*. 2010;10(6):387-94.
8. Visser ME, Stead MC, Walz G, Warren R, Schomaker M, et al. Baseline predictors of sputum culture conversion in pulmonary tuberculosis: Importance of cavities, smoking, time to detection and w-beijing genotype. *PLoS ONE*. [doi:10.1371/journal.pone.0029588]. 2012;7(1): e29588.
9. Tiwari S, Kumar A, Kapoor SK. Relationship between sputum smear grading and smear conversion rate and treatment outcome in the patients of pulmonary tuberculosis undergoing dots--a prospective cohort study. *Indian J Tuberc*. 2012 Jul;59(3):135-40.
10. Banu Rekha VV, Balasubramanian R, Swaminathan S, Ramachandran R, Rahman F, Sundaram V, et al. Sputum conversion at the end of intensive phase of category-1 regimen in the treatment of pulmonary tuberculosis patients with diabetes mellitus or hiv infection: An analysis of risk factors. *Indian J Med Res*. 2007;126(5):452-8.
11. Kayigamba FR, Bakker MI, Mugisha V, De Naeyer L, Gasana M et al. Adherence to tuberculosis treatment, sputum smear conversion and mortality: A retrospective cohort study in 48 rwandan clinics. *PLoS ONE*. [Article]. 2013;8(9):1-10.
12. Caetano Mota P, Carvalho A, Valente I. Predictors of delayed sputum smear and culture conversion among a portuguese population with pulmonary tuberculosis. *Revista Portuguesa de Pneumologia (English Edition)*. 2012;18(2):72-9.
13. Rieder HL. Sputum smear conversion during directly observed treatment for tuberculosis. *Tubercle and Lung Disease*. 1996;77(2):124-9.
14. Bawri S, Ali S, Phukan C, Tayal B. A study of sputum conversion in new smear positive pulmonary tuberculosis cases at the monthly intervals of 1, 2 & 3 month under directly observed treatment, short course (dots) regimen. *Lung India*. 2008;25(3):118-23. doi: 10.4103/0970-2113.44122.
15. Bouti K, Aharmim M, Marc K, Soualhi M, Zahraoui R, Benamor J, et al. Factors influencing sputum conversion among smear-positive pulmonary tuberculosis patients in morocco. *ISRN Pulmonology*. 2013;2013:5.
16. Senkoro M, Mfinanga SG, Mørkve O. Smear microscopy and culture conversion rates among smear positive pulmonary tuberculosis patients by hiv status in dar es salaam, tanzania. *BMC infectious diseases*. 2010;10(1):210.
17. Güler M, Ünsal E, Dursun B, Aydın Ö, Capan N. Factors influencing sputum smear and culture conversion time among patients with new case pulmonary tuberculosis. *International journal of clinical practice*. 2007;61(2):231-5.
18. Parikh R, Nataraj G, Kanade S. Time to sputum conversion in smear positive pulmonary tb patients on category i dots and factors delaying it. *J Assoc Physicians India*. 2012;60:22-6.

