

## **SURAT KETERANGAN**

Nomor: 1901/UNUSA-LPPM/Adm.I/IX/2022

Lembaga Penelitian dan Pengabdian Kepada Masyarakat (LPPM) Universitas Nahdlatul Ulama Surabaya menerangkan telah selesai melakukan pemeriksaan duplikasi dengan membandingkan artikel-artikel lain menggunakan perangkat lunak **Turnitin** pada tanggal 21 September 2022.

Judul : Sputum Smear Conversion as Prognostic Determinant of Timely Complete Therapy on Pulmonary Tuberculosis

Penulis : Bastiana, Muzajadah Retno Arimbi

No. Pemeriksaan : 2022.09.19.753

Dengan Hasil sebagai Berikut:

**Tingkat Kesamaan diseluruh artikel (*Similarity Index*) yaitu 8%**

Demikian surat keterangan ini dibuat untuk digunakan sebagaimana mestinya.

Surabaya, 21 September 2022

Ketua LPPM



UNUSA  
LPPM

Achmad Syafiuddin, Ph.D

NPP: 20071300

**LPPM Universitas Nahdlatul Ulama Surabaya**

Website : lppm.unusa.ac.id

Email : lppm@unusa.ac.id

Hotline : 0838.5706.3867

# Sputum Smear Conversion as Prognostic Determinant of Timely Complete Therapy on Pulmonary Tuberculosis

*by* BastianaBastiana

---

**Submission date:** 21-Sep-2022 10:23AM (UTC+0700)

**Submission ID:** 1905088783

**File name:** 1974-6253-1-PB.pdf (523.32K)

**Word count:** 3689

**Character count:** 19026

## Sputum Smear Conversion as Prognostic Determinant of Timely Complete Therapy on Pulmonary Tuberculosis

Bastiana<sup>1</sup>, Muzajadah Retno Arimbi<sup>2</sup>

<sup>1</sup>Department of Clinical Pathology, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya/Islamic Hospital Jemursari, Surabaya, Indonesia. E-mail: [dr.bastiana@unusa.ac.id](mailto:dr.bastiana@unusa.ac.id)

<sup>2</sup>Department of Pulmonology, Faculty of Medicine, Universitas Wijaya Kusuma Surabaya/Islamic Hospital Jemursari, Surabaya, Indonesia

### ABSTRACT

Tuberculosis (TB) remains a major health problem worldwide. The bacteriological diagnosis of TB is confirmed by a sputum smear, which shows a positive result. Sputum culture conversion at two months of TB therapy has a higher possibility of completing therapy; however, this method is time-consuming and expensive. This study aimed to analyze the initial smear and smear conversion of sputum in the intensive phase therapy as a prognostic determinant of appropriate time-targeted therapy. This was a retrospective study on pulmonary TB patients collected from January 2016 to December 2017. The research subjects at the beginning of the intensive phase were divided into Acid-Fast Bacilli (AFB)-negative and AFB-positive (1+, 2+, 3+) sputum smears. The sputum smear examination was evaluated at the end of the intensive phase and the end of the six-month treatment. The pulmonary TB patients in this study were 430 patients, dominated by males with the main distribution age of 45-54 years. At the beginning of the intensive phase, the negative results of the AFB examination were 85.4% and the total positive results with 1+, 2+, or 3+ were 14.6%. At the end of the intensive phase, the sputum smear examination of all patients showed 100% conversion, and the sputum smear examination at the end of six months of treatment showed negative results. This study has revealed that sputum conversion at the end of the 2-month intensive phase can be used as a prognostic determinant of timely complete therapy on pulmonary tuberculosis.

**Keywords:** Pulmonary tuberculosis, sputum smear conversion, prognostic determinant

### INTRODUCTION

Tuberculosis (TB) remains a world health problem that requires serious attention. It was estimated that there were more than 10 million TB patients in 2019 worldwide. The World Health Organization (WHO) reported that the majority of TB patients in 2019 were in Southeast Asia (44%), Africa (25%) and the Western Pacific (18%). Indonesia is listed as the country with the second largest TB burden in the world (8.5%) after India (26%) and above China (8.4%).<sup>1</sup>

Early TB diagnosis is commonly difficult in clinical practice, and early detection of pulmonary TB remains a challenge for clinicians. Prompt diagnosis of active pulmonary TB is a priority to control the spread of TB both for individual treatment and for public health intervention to reduce the further spread in the community. The diagnosis of TB can be confirmed in several ways, including Chest X-ray/imaging, Ziehl-Neelsen acid-fast bacteria staining, TB culture, and nuclear amplification and gene-based test.<sup>2</sup> The diagnosis of TB in Indonesia is established in two ways, such as bacteriological and clinical

diagnosis based on medical history and chest X-ray/imaging. Bacteriological diagnosis is established when: a positive sputum smear is found; through a rapid molecular test for instance using Xpert MTB/RIF, or through a TB culture test. The diagnosis is made clinically with clinical findings and chest X-ray/imaging when the AFB sputum smears are negative.<sup>3</sup>

The Sputum Conversion Rate (SCR) using random sputum is defined as the percentage of smear-positive pulmonary TB cases listed in a specified period that converted to smear-negative status after the standard two months of the intensive phase of treatment. Delayed sputum-smear conversion-related factors were wide, including CXR findings in diagnosis, age range >60, treatment enrolment, smoking behavior, no directly observed treatment short-course observer, foreign citizens, and suburban home locations.<sup>4</sup> The escalation of screening and diagnostic testing followed by eradication of undernutrition, poverty, diabetes, smoking, and air pollution need to be addressed to achieve WHO 2035 TB care and prevention targets.<sup>5</sup> Previous research in a few Nigerian hospitals stated that sputum culture

conversion at two months of TB therapy increased the probability to complete therapy on time.<sup>6</sup> In addition, factors enhancing treatment adherence and lowering infectiousness after initial treatment improved health literacy among the community.<sup>7</sup>

Studies<sup>2</sup> on sputum smear conversion in pulmonary TB patients have frequently been reported in some countries; however, the research on initial sputum smear status and sputum conversion as prognostic determinants of timely complete therapy of pulmonary TB patients has never been reported. Therefore, the purpose of this study was to analyze<sup>8</sup> sputum smear in the early intensive phase and the sputum smear conversion at the end of the intensive phase of pulmonary TB patients as a prognostic determinant of the timely complete therapy.

## METHODS

This was observational analytical research using a retrospective data collection in all TB patients at the Pulmonary clinic of Islamic Hospital Jemursari Surabaya, both from the Acid-Fast Bacilli (AFB) positive sputum smear and negative sputum smear. The inclusion criteria were as follows: Patients diagnosed bacteriologically or clinically with pulmonary TB by a Pulmonologist; The examination of positive sputum smear and negative sputum smear validated by a Clinical Pathologist; Patients who qualified the criteria for category I of TB therapy; Patients who underwent treatment for at least 6 months. The exclusion criteria were TB patients with uncontrolled diabetes mellitus, HIV, and TB patients with malignancy.

The diagnosis of pulmonary tuberculosis in patients clinically was performed by using medical history of suspected criteria of cough for more than 2 weeks, loss of appetite or body weight, and fever, including additional tests such as chest X-ray.<sup>3</sup> The results of TB diagnosis were obtained when there were clinically and radiologically fibroinfiltrates, fibroindurations, and cavities. The AFB sputum from pulmonary tuberculosis patients was collected at the beginning of intensive therapy, and the end of intensive and 6-month therapy using the Ziehl Neelsen staining method. The results of the AFB examination were reported<sup>11</sup> positive when AFB were found, categorized in AFB 1+ (10-99 AFB per 100 fields), 2+ (1-10 AFB per field), and 3+ (more than 10 AFB per field). The treatment process for category I TB patients was carried out with a single dose multidrug therapy method for 6-months. Final evaluation of AFB sputum smears status and the

outcome therapy of patients (cured in 6-month therapy or need to continue the treatment to 9-month therapy/prolonged) was carried out after 6-months of therapy. The patient was declared cured/complete therapy or prolonged by a Pulmonologist based on clinical, laboratory, and radiological data of the patients.

Univariate data in the form of frequency distribution data were presented. The SCR was calculated by the proportion of converted sputum smear with all patients in<sup>9</sup> the intensive phase. The correlation between the conversion of AFB sputum at the end of the intensive phase with the patient outcome of 6-months of complete therapy and the correlation between the AFB sputum at the beginning of the intensive phase with the patient outcome of 6-months of complete therapy in pulmonary TB patients were statistically analyzed by Chi-Square<sup>2</sup> test by using statistical software SPSS version 25. Research permission was obtained from the Health Research Ethics Committee of Islamic Hospital Jemursari, Surabaya with number 00198/KEPK-RSUIS/IV/2018.

## RESULTS AND DISCUSSIONS

A total of 430 pulmonary TB patients in this study was collected from January 2016 to December 2017<sup>13</sup> the age ranging from 15 to 83 years old (Table 1).

**Table 1.** Characteristics of patients with pulmonary TB

Age	Patients (n)	Gender Category	
		Male (n)	Female (n)
15-24	48	21	27
25-34	80	32	48
35-44	82	49	33
45-54	85	55	30
55-64	72	43	29
>65	63	49	14
<b>Total</b>	<b>430</b>	<b>249</b>	<b>181</b>

There were 249 male patients (57.9%) and 181 female patients (42.1%) involved in this study. This study showed that most pulmonary TB patients were dominated by males with the main distribution age of 45-54 years. Studies conducted by China indicated that the incidence of TB increased from year to year at the age of 45 and over, with the highest number of sufferers aged 15-24.<sup>8</sup> TB infection closely related to increase, earlier study stated that the highest prevalence was in the 65 year and over.<sup>9</sup>

Regarding AFB examination at the beginning of intensive therapy, 366 patients were negative (85.1%), 32 patients were 1+ (7.4%), 15 patients were 2+ (3.5%) and 17 patients were 3+ (4%). The AFB sputum at the end of the intensive phase of therapy was examined, and the conversion was calculated for evaluation of the therapy outcome. Table 2 presents the initial AFB data and AFB conversion at the end of the two months intensive phase of therapy.

As described in Table 2, the result of AFB conversion of all patients was 100%. A negative AFB sputum result indicated that the patient was no longer infectious. The total sputum conversion rate in all groups of pulmonary TB patients reached 100%. The results of AFB at the end of the 6-month treatment can be seen in Table 3.

The all group of patients at the end of 6-months of treatment showed negative AFB results of 100%, respectively. There were 100% of patients with a

negative smear result in the group of patients with a positive initial smear and the group with a negative initial smear at the end of 6-month treatment.

From Table 4, it can be seen that from 366 patients with negative initial AFB status, 335 patients were declared cured within 6 months of therapy; therefore, the cure rate at 6 months of therapy in the group of patients with negative initial AFB was  $335/366 \times 100\%$ , totaling 91.5%. A total of 31 patients were included in the 9-month treatment category. This study showed that the group of patients with negative initial AFB status had a 91.5% cure rate during the duration of 6-month complete therapy, and a small proportion (31 subjects) of this patient group was classified into the 9-month treatment category and showed a 100% cure rate at the end of treatment.

From Table 4 it can also be seen that from 32 patients with initial AFB status 1+, there were 32

**Table 2.** Initial and 2-month intensive phase therapy of AFB smear

	Initial AFB Smear	Negative AFB Smear at the End of Intensive Phase (2 months)	AFB Conversion (%)
Negative	366	366	100
1+	32	32	100
2+	15	15	100
3+	17	17	100
<b>Total</b>	<b>430</b>	<b>430</b>	<b>100</b>

**Table 3.** Results of AFB smears at the end of 6-month treatment

	Initial AFB Smear	Negative AFB Smear at the End of 6-Month Therapy	Percentage of Negative AFB (%)
Negative	366	366	100
1+	32	32	100
2+	15	15	100
3+	17	17	100
<b>Total</b>	<b>430</b>	<b>430</b>	<b>100</b>

**Table 4.** Sputum AFB at the beginning of the intensive phase and patient outcome after 6-month complete therapy

	Initial AFB Smear	Negative AFB Smear at the End of 6-Month Therapy	Completing 6-Month of TB Therapy (cured)	Extending anti-TB Treatment to 9-Months (prolonged)
Negative	366	366	335	31
1+	32	32	31	1
2+	15	15	14	1
3+	17	17	16	1
<b>Total</b>	<b>430</b>	<b>430</b>	<b>396</b>	<b>34</b>

patients whose AFB results became negative and 31 were declared cured within 6 months of therapy; therefore, the cure rate at 6 months of therapy in the group of patients with 1+ initial AFB was 31/32x 100%, totaling 96.8%.

In the group of patients with baseline AFB 2+, all 15 patients with baseline AFB 2+ showed negative AFB after 6 months of therapy and 14 patients were declared cured; therefore, the cure rate was 14/15 x 100%, totaling 93.3%. Likewise, in the group of patients with initial AFB 3+, their cure rate was 16/17 x 100%, totaling 94.1%. The total number of patients with positive baseline AFB who recovered within 6 months of therapy was 61/64 x 100%, totaling 95.3%. This study revealed that the group of patients with a positive initial smear of 1+, 2+ or 3+ had a cure rate of 95.3% in 6-month therapy.

The total number of patients with a 6-month complete therapy in the initial negative and positive baseline AFB group was 396/430 x 100%, totaling 92.1%. The total number of patients with 9-month complete therapy was 34/430 x 100%, totaling 7.9%.

The correlation between the initial intensive phase of sputum smear and the outcome of 6-month therapy in pulmonary tuberculosis patients in this study was statistically analyzed using the Chi-Square test ( $\alpha=0.05$ ). In this analysis, the groups will be divided into the negative and the positive (1+, 2+, or 3+) groups at the beginning of the intensive phase.

As described in Table 5, the p-value was 0.301 > 0.05. This indicated that there was no significant correlation between the initial intensive AFB with the patient outcome of 6-months complete therapy. Whatever the results of the initial intensive phase of AFB sputum status, both the negative and positive AFB smear results (+1, +2, and +3) did not

affect the outcome of complete therapy (6 months). The results of this study showed a high percentage of patients completing 6-month therapy and declared cured regardless of the initial results of the patient's AFB smear.

This study showed good results despite the presence of negative sputum and positive sputum with grades 1+, 2+ and 3+ at the beginning. Another study found a bacillary load that was indicated to be 2+ or 3+ indicated conversion failure at the end of the intensive phase.<sup>10</sup> Increased completed treatment on culture-positive cases suggests improved case management and strengthened cases belonging to the population.<sup>11</sup> In line with this research, a study conducted in Ethiopia showed a 75% cure rate in smear-positive patients that the treatment outcome was affected by age, distance to the health facility, and serostatus of HIV.<sup>12</sup>

Regarding the relation between the smear sputum conversion at the end of a intensive phase and patient recovery, this analysis was divided into two groups such as the sputum conversion group at the end of the intensive phase and the non-conversion group, either +1, +2, or +3 using Chi-Square test (Table 6).

The p-value could not be analyzed because all sputum examinations at the end of the intensive phase were negative. All AFB sputum smear examinations were converted at the end of the intensive phase.

This study suggested that AFB sputum smears at the end of the intensive phase in the group of patients with initial AFB status of 1 +, 2 +, and 3 + showed 100% of conversion. The cure rate of 6-month complete therapy in this patient group was 95.3%. Three (3) patients had to undergo 9-month

**Table 5.** Chi-Square analysis of initial AFB smear and 6-month complete therapy

		Patient Outcome at 6-Month Therapy			
		Cured	Not Cured	Total	p-value
<b>Initial Sputum Smear</b>	Negative	335	31	366	0.301
	Positive (1+, 2+, 3+)	61	3	64	
	<b>Total</b>	396	34	430	

**Table 6.** Chi-Square analysis of AFB conversion and outcome of 6-month therapy

		Patient Outcome at 6-Month Therapy			
		Cured	Not Cured	Total	p-value
<b>End of 2-month intensive sputum smear</b>	Sputum conversion	396	34	430	-
	No conversion (1+, 2+, 3+)	0	0	0	
	<b>Total</b>	396	34	430	

therapy and showed a 100% cure rate at the end of the treatment. The total AFB conversion rate of this patient group was 100% and almost 100% had the 6-month complete therapy. From these data, it was concluded that the sputum conversion at the end of the intensive phase can be used as a prognostic determinant of 6-month complete therapy on time in pulmonary TB patients.

This study was in line with previous studies in Cameroon, which stated that sputum conversion at the end of the intensive phase of therapy has a better therapeutic outcome than those who did not perform sputum conversion.<sup>6</sup> A study conducted on MDR-TB patients with a bi-monthly treatment evaluation method with sputum culture conversion stated that conversion in the first two months of treatment had a better therapeutic outcome than patients without conversion.<sup>13</sup> Another study conducted on MDR-TB patients with DM and without DM showed no significant difference in conversion culture time between both populations and both had the same chance of recovery.<sup>14</sup>

Some factors play a role in patient recovery including marital status, HIV status, level of education, treatment category, and knowledge.<sup>15</sup> Several factors that can cause the failure of TB therapy are the delay in the initiation of intensive therapy from initial symptoms, which are weight loss, the delay in the late intensive phase smear, and the high bacilli load at the end of the intensive phase.<sup>16</sup>

This study revealed that there was a total increase or no more bacillary load found on AFB smears at the end of the intensive phase. The majority of patients who were admitted and recovered within 6 months of therapy had demonstrated sputum conversion into negative results at the end of the intensive phase. This suggested that sputum conversion at the end of the intensive phase can be used as a prognostic determinant of the appropriateness of 6-months complete TB therapy on time. In addition, this study also found that the initial sputum smear status, both smear-positive (+1, +2, and +3) and smear-negative showed no significant difference in terms of the prognosis of complete therapy on time.

## CONCLUSIONS AND SUGGESTIONS

Sputum conversion in patients with pulmonary TB in the intensive phase can be used as a prognostic determinant of complete therapy on time after 6-months of treatment for TB patients. The patient's initial AFB status did not affect the accuracy of the

on-time recovery, almost all patients showed on-time recovery. A further longitudinal cohort study was needed to evaluate the etiological factors in patients who had prolonged 9-month therapy.

## ACKNOWLEDGEMENTS

The authors would like to thank M. Auzan Ferdiansyah and Prima Ardiansah Surya for their generous support and encouragement during the preparation of the manuscript, and Universitas Nahdlatul Ulama Surabaya for providing the research fund.

## REFERENCES

1. Global tuberculosis report. Geneva, World Health Organization, 2020. Available from: <https://apps.who.int/> (accessed 10 April 2021).
2. Kon OM (Ed). Tuberculosis in clinical practices. Switzerland AG, Springer Nature, 2021; 29-52.
3. Peraturan Menteri Kesehatan Republik Indonesia nomor 67 tahun 2016 tentang penanggulangan Tuberculosis. 2021. Available from: <http://hukor.kemkes.go.id/> (accessed 10 April, 2021).
4. Mokti K, Isa Z, Sharip J, Bakar SNA, Atil A, et al. Predictors of delayed sputum smear conversion among pulmonary tuberculosis patients in Kota Kinabalu, Malaysia: A retrospective cohort study. *Medicine (Baltimore)*, 2021; 100(31): e26841.
5. Chakaya J, Khan M, Ntoumi F, Akililu E, Fatima R, et al. Global tuberculosis report 2020—reflections on the global TB burden, treatment and prevention efforts. *International Journal Infectious Disease*, 2020; 1(1): S7-S12.
6. Ige O, Oladoku R. Time to sputum culture conversion as a prognostic marker for end-of-treatment outcome is the first cohort of MDR-TB patients managed in a Nigerian tertiary hospital. *European Respiratory Journal*, 2016; 48: 60.
7. Asemahagn MA. Sputum smear conversion and associated factors among smear-positive pulmonary tuberculosis patients in East Gojjam Zone, Northwest Ethiopia: A longitudinal study. *BMC Pulmonary Medicine*, 2021; 21: 118.
8. Zhu M, Han G, Takiff H, Wang J, Ma J, Zhang M, Liu S. Times series analysis of age-specific tuberculosis at a rapid developing region in China, 2011-2016. *Scientific Reports Nature Research*, 2018; 8: 8727.
9. Noviyani A, Nopsoyon T, Pongpirul K. Variation of tuberculosis prevalence across diagnostic approaches and geographical areas of Indonesia. *PLoS One*, 2021; 16(10): e0258809.
10. Djouma F, Noubom M, Ateudijieu J, Donfack H. Delay in sputum smear conversion and outcomes of smear-positive tuberculosis patients: A retrospective cohort study in Bafoussam, Cameroon. *BMC Infectious Diseases*, 2015; 15: 139.

11. Guthman JP, Leon L, Antoine D, Levy-Bruhl D. Tuberculosis treatment outcomes of notified cases: trends and determinants of potential unfavorable outcome, France, 2008 to 2014. *Eurosurveillance*, 2020; 25(4):1900191.
12. Tesema T, Seyoum D, Ejeta E, Tsegaye R. Determinants of tuberculosis treatment outcome under directly observed treatment short courses in Adama City, Ethiopia. *PLoS ONE*, 2020; 15(04): e0232468.
13. Kurbatova E, Cegielski J, Lienhardt C, Akksilp R, Bayona J, *et al*. Evaluation of sputum culture conversion as a prognostic marker for end-of-treatment outcome in patients with multidrug-resistant tuberculosis. *Lancet Respiratory Medicine*, 2015; 3(3):201-209.
14. Fauziah H, Aprianti S, Handayani I, Kadir NA. Analysis of smear microscopy and culture conversion results in multidrug-resistant tuberculosis patients with and without type 2 diabetes mellitus. *Indones J Clin Pathol Med Lab*, 2020; 26(3):272-76.
15. Ali M, Karanja S, Karama M. Factors associated with tuberculosis treatment outcomes among tuberculosis patients attending tuberculosis treatment centers in 2016-2017 in Mogadishu, Somalia. *Pan African Medical Journal*, 2017; 28:197.
16. Diallo A, Dahourou D, Dah T, Tassebedo S, Sawadogo R, Meda N. Factors associated with tuberculosis treatment failure in the Central East Health regimen of Burkina Faso. *The Pan African Medical Journal*, 2018; 30:293.



# Sputum Smear Conversion as Prognostic Determinant of Timely Complete Therapy on Pulmonary Tuberculosis

## ORIGINALITY REPORT

16%

SIMILARITY INDEX

15%

INTERNET SOURCES

13%

PUBLICATIONS

9%

STUDENT PAPERS

## PRIMARY SOURCES

1	<a href="http://www.researchgate.net">www.researchgate.net</a> Internet Source	3%
2	<a href="http://www.indonesianjournalofclinicalpathology.org">www.indonesianjournalofclinicalpathology.org</a> Internet Source	3%
3	Eric Walter Pefura-Yone, André Pascal Kengne, Christopher Kuaban. "Non-conversion of sputum culture among patients with smear positive pulmonary tuberculosis in Cameroon: a prospective cohort study", BMC Infectious Diseases, 2014 Publication	2%
4	Submitted to Sriwijaya University Student Paper	1%
5	Submitted to Ain Shams University Student Paper	1%
6	<a href="http://bm Cresnotes.biomedcentral.com">bm Cresnotes.biomedcentral.com</a> Internet Source	1%
7	Kefyalew Addis Alene, Kerri Viney, Hengzhong Yi, Emma S. McBryde et al. "Comparison of	1%

the validity of smear and culture conversion as a prognostic marker of treatment outcome in patients with multidrug-resistant tuberculosis", PLOS ONE, 2018

Publication

- 
- |    |   |     |
|----|---|-----|
| 8  | <a href="https://journals.lww.com">journals.lww.com</a><br>Internet Source  | 1 % |
| 9  | Submitted to Universiti Sains Malaysia<br>Student Paper   | 1 % |
| 10 | Djouma, Fabrice Nembot, Michel Noubom, Jérôme Ateudjieu, and Hubert Donfack. "Delay in sputum smear conversion and outcomes of smear-positive tuberculosis patients: a retrospective cohort study in Bafoussam, Cameroon", BMC Infectious Diseases, 2015.<br>Publication                              | 1 % |
| 11 | <a href="https://journals.plos.org">journals.plos.org</a><br>Internet Source  | 1 % |
| 12 | Zohra Bhatti, Amer Hayat Khan, Syed Azhar Syed Sulaiman, Madeeha Laghari, Irfhan Ali Bin Hyder Ali. "Determining the risk factors associated with delayed sputum conversion at the end of the intensive phase among tuberculosis patients", Eastern Mediterranean Health Journal, 2021<br>Publication | 1 % |
| 13 | <a href="https://onlinelibrary.wiley.com">onlinelibrary.wiley.com</a><br>Internet Source  |     |
-

1 %

14

researchspace.ukzn.ac.za

Internet Source

1 %

Exclude quotes On

Exclude matches < 1%

Exclude bibliography On