

## Predictors of smear non-conversion among new-treatment pulmonary tuberculosis: a single center case-control study in Indonesia

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### ABSTRACT

**BACKGROUND** Previous studies concluded predictors of smear non-conversion pulmonary tuberculosis (TB) globally as well as in Indonesia. However, there is a limited data in hospital setting. This study aimed to explore predictors of smear non-conversion pulmonary TB in hospital setting.

**METHODS** A case-control study was conducted to explore predictors of smear non-conversion among new-treatment pulmonary TB in Dr. Kariadi General Hospital from 2017 to 2019. Number of cases and controls have been determined consecutively. Data were collected from secondary data accessed in medical records and directly from subjects. Non-conversion status in the case group was defined as a persistent sputum smear-positive after 2 months of intensive phase of treatment. The subjects' characteristics i.e., age, sex, body mass index, education level, occupational status, and predictors of smear non-conversion, i.e., patient's compliance, smoking status, alcohol consumption, presence of drugs side effects, health care access, first acid-fast bacilli (AFB) smear grading, diabetes mellitus (DM), housing condition, housing density, and household income were observed. Chi-square test and binary logistic regression were used.

**RESULTS** 35 subjects were determined in the case group while 76 subjects were the control group and involved in the final analysis. Age, sex, first AFB smear grading, smoking status, housing condition, housing density, and DM were involved in the model of logistic regression. DM (OR = 3.4; 95% CI = 1.19–10.00) and first AFB smear grading (OR = 11.2; 95% CI = 3.86–33.00) were concluded as the predictors of smear non-conversion.

**CONCLUSIONS** DM and first AFB smear grading were the predictors of smear non-conversion among new-treatment pulmonary TB subjects.

**KEYWORDS** microbiological techniques, Mycobacterium, pulmonary tuberculosis

Tuberculosis (TB) remains a serious public health problem, which includes in the top 10 causes of death in the world.<sup>1</sup> An estimated 10 million people got pulmonary TB and 1.2 million of them died in 2018.<sup>1</sup> Geographically, most of the TB cases occur in Asia (44%). Indonesia ranks third (8%), after India (27%) and China (9%), which contributes the most TB cases in the world.<sup>1</sup> Surprisingly, TB cases in Indonesia

increased by 70%, from 331,703 in 2015 to 563,879 in 2018.<sup>1</sup> The failure in the management of pulmonary TB was highly caused by limited resources, low quality of health system, and high HIV infection rate.<sup>1,2</sup>

The critical parameters in evaluating pulmonary TB management are cure rate and smear conversion rate.<sup>3</sup> In 2018, TB cure rate in Indonesia was 71.08% which

was lower than 85%, the rate determined by World Health Organization.<sup>1</sup> Smear conversion rate was also decreased remarkably from 80.6% in 2013 to 50.5% in 2014.<sup>1</sup>

The decrease of smear conversion rate adjusts with the increase of smear non-conversion rate. Smear non-conversion will make the treatment longer and increase the risk of drug resistance, relapse, and mortality, as well as the TB transmission to others.<sup>4</sup> It has been proven that some factors, i.e., patient's compliance,<sup>3,5,6</sup> smoking status,<sup>3,7</sup> diabetes mellitus (DM),<sup>8</sup> HIV co-infection,<sup>9</sup> and smear acid-fast bacilli (AFB) grading<sup>9</sup> are associated with smear non-conversion pulmonary TB. Studies also showed that the conversion rate in Persahabatan General Hospital, Jakarta, Indonesia was 90.8% in 2014<sup>10</sup> and Sri Venkateswara Ramnarain Ruia Government General Hospital, Tirupati, India was 90.4%.<sup>11</sup> However, the studies did not analyze the risk factors. Additionally, other studies reported that drug side effects,<sup>12</sup> alcohol consumption,<sup>13</sup> health care access,<sup>14</sup> household income,<sup>13</sup> and housing characteristics<sup>15,16</sup> i.e., housing condition, and housing density were associated with TB treatment outcome.

Previous studies<sup>3,7,9,17</sup> concluded the risk factors of smear non-conversion in TB. However, to the best of our knowledge, there is still a lack of data regarding the relationship between drug side effects, alcohol consumption, household income, health care access, housing characteristics, and smear non-conversion; moreover, a few data are known in the Indonesian hospital setting. This study aimed to explore the predictors of smear non-conversion pulmonary TB.

## METHODS

This case-control study was conducted from 2017 to 2019. The secondary data were taken from medical records and TB patients' monitoring sheets, whereas the primary data were collected from an interview and observation of the subjects recorded in the pulmonary TB registry in Dr. Kariadi General Hospital. All procedures performed in this study were approved by the Institutional Review Board Committee, Department of Public Health, Universitas Negeri Semarang (No.052/KEPK/EC/2019). All subjects involved in the study provided informed consent. The sample size was determined to meet the minimum sample according to the formula for a case-control

study published previously.<sup>18</sup> Thirty subjects with smear non-conversion of new-treatment pulmonary TB were assigned as a case group, meanwhile twice were assigned in the control group. Both of the groups were added a minimum of 10% for the anticipation of incompleteness, rejection, and another thing.

Non-conversion status was defined as a persistent sputum smear-positive after 2 months of the intensive phase of treatment. It was categorized as the case group. Smear examinations were conducted for three sputum smear specimens, i.e., first spot, second spot, and morning sample sputum. Results were determined as positive if at least one of the specimens was positive, while negative if all of them were negative. Subjects with negative results then were categorized as the control group. This study included subjects aged more than or equal to 15 years old. Subjects with extra-pulmonary TB, HIV/AIDS, or re-treatment status were excluded from the study.

A number of 674 subjects had TB directly observed a short-course treatment, which was recorded in Dr. Kariadi General Hospital TB registry from 2017 to 2019. Meanwhile, there were 254 subjects diagnosed pulmonary TB with positive AFB. Among them, 209 subjects were diagnosed with conversion status. Subjects in the control group were obtained sequentially from the last visit to the hospital until the number was obtained as determined. The detailed study subjects' recruitment is illustrated in Figure 1.

Secondary data were collected to determine the smear non-conversion status and subjects' characteristics. The subjects' characteristics include age, sex, body mass index (BMI), level of education, and occupational status. Level of education is categorized as high and low. High-level education is for subject who passed high school or above. The study also observed determinants of non-conversion pulmonary TB, i.e., patient's compliance, smoking status, alcohol consumption, the presence of drugs side effects, health care access, first AFB smear grading, DM, housing condition, housing density, and household income. These parameters were collected directly from subjects, except AFB smear grading.

Patients who paused the treatment for  $\geq 1$  weeks consecutively or a total interruption of 12 days in non-consecutive days were considered as non-compliers. Current or former alcohol routine usage in any dosage

and frequency was categorized as alcohol user as well as a current and former smoker. The presence of drug side effects involved the presence of the subjects' complaints after medication, i.e., nausea, itching, arthralgia, hearing disorder, anorexia, and abnormal urine color. The limitation of health service access was determined by cost and distance.

AFB examination was conducted by the clinical microbiologist in the Clinical Microbiology Laboratory, Central Laboratory Unit, Dr. Kariadi General Hospital. The data were obtained from medical records. The AFB were stratified into: 0: nil, 1+:  $\leq 1$  AFB, 2+: 2–9 AFB, 3+:  $\geq 10$  AFB per 10 fields of view, respectively. AFB smear ratings were categorized as high if the results were either 3+ or 2+ and low if the results were either 1+ or scanty.

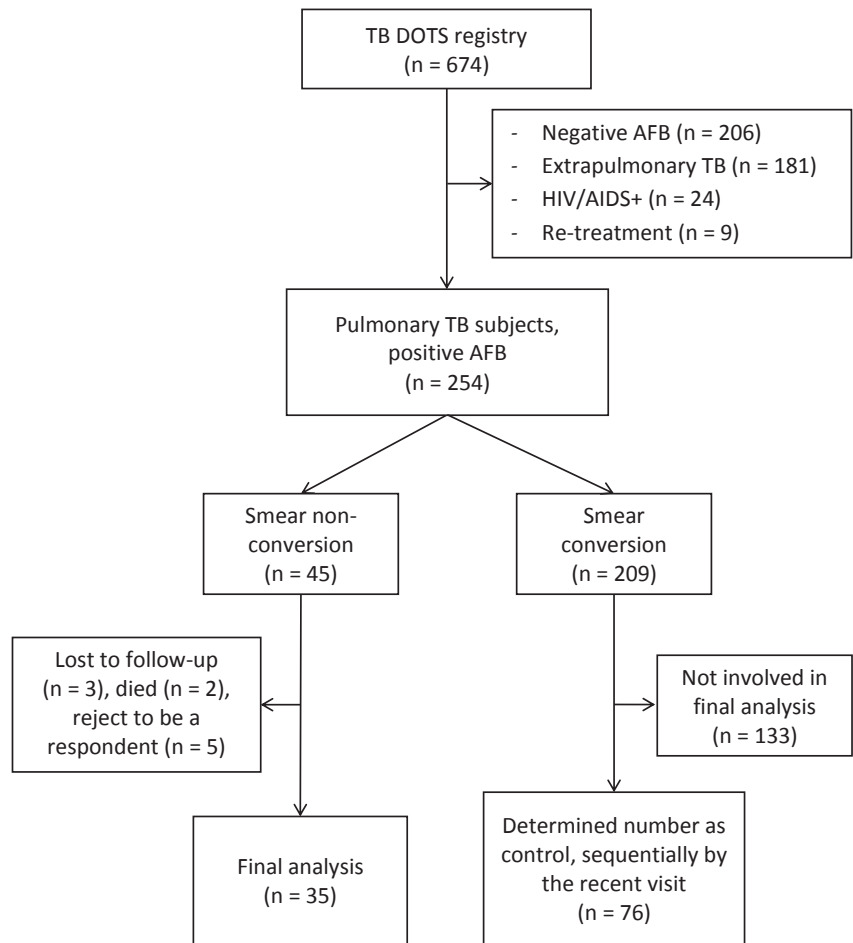
The housing condition consists of wall conditions, floor conditions, and lighting. The housing density was determined as a number of the building area divided by a number of family members living in the same house. The condition that met the criterion as published in previous study<sup>15</sup> was used to determine the status.

Household income was considered fair when it met the regional minimum salary determined by the local government.

Data were presented in frequency and percentage based on the case and the control group. Chi-square test was performed to analyze the association of predictors and the smear non-conversion pulmonary TB status. A *p*-value  $< 0.05$  was considered as statistically significant. The predictors with a *p*-value lower than 0.25 were involved in the logistic regression analysis. All statistical analysis was performed using SPSS software version 16.0 (IBM Corp., USA).

## RESULTS

Of the 45 non-conversion subjects were in the case group; however, only 35 subjects completed primary and secondary data (Figure 1). A total of 76 subjects with smear conversion was determined as the control group. The subjects' characteristics, i.e., age, sex, level of education, and occupational status based on case and control group, are presented in



**Figure 1.** Subjects recruitment. TB=tuberculosis; DOTS=directly observed treatment short-course; AFB=acid-fast bacilli

Table 1. In the non-conversion group, the proportion of older subjects was higher than younger. Regarding the gender, males were higher than females for the non-conversion group. The level of education and occupational status were comparable between the groups.

**Table 1.** Subject's characteristics

Characteristics	Non-conversion status		p*
	Yes, n (%) (N = 35)	No, n (%) (N = 76)	
Age (years)			<b>0.013</b>
≥55	20 (57)	23 (30)	
15–54	15 (43)	53 (70)	
Male sex	24 (69)	37 (49)	0.080
Level of education			0.499
Low	6 (17)	19 (25)	
High	29 (83)	57 (75)	
Occupational status			0.566
Unemployed	12 (34)	32 (42)	
Employee	23 (66)	44 (58)	

\*Chi-square test

Predictors of smear non-conversion status pulmonary TB as stated in Table 2 reveals that the proportion of non-conversion group was significantly higher in first AFB smear grading ≥2+. BMI and drug side effects between groups were comparable, whereas the smoking status of the non-conversion group was higher. Surprisingly, the proportion of DM was lower compared to the non-DM for both conversion status; however, the proportion of both was significantly different. The other five predictors namely alcohol consumption, access to the health services, housing condition, housing density, and household income were comparable between groups.

Table 2 also shows the results of binary logistic regression. The final model concluded that DM and high smear grading were significantly predicting smear non-conversion status among new-treatment pulmonary TB with a contribution of 68.19% and the rest 31.81% influenced by other predictors. DM predicts non-conversion with an adjusted odds ratio (OR) was 3.44, while high smear grading predicts non-conversion with an adjusted OR was 11.22.

**Table 2.** Predictors for smear non-conversion status pulmonary TB

Predictors	Non-conversion status		p*	OR (95% CI)	p†	Adjusted OR (95% CI)
	Yes, n (%) (N = 35)	No, n (%) (N = 76)				
First AFB smear grading			<b>&lt;0.001</b>		<b>&lt;0.001</b>	
≥2+	29 (83)	20 (26)		13.533 (4.897–37.401)		11.223 (3.861–33.007)
<2+	6 (17)	56 (74)		1.00		1.00
BMI (kg/m <sup>2</sup> )						
Underweight (<18.5)	14 (40)	27 (36)	0.616	1.383 (0.575–3.323)	-	-
Overweight (>23)	6 (17)	9 (12)	0.525	0.562 (0.171–1.851)	-	-
Normal (18.5–23)	15 (43)	40 (53)	1.00	1.00	-	-
Had drugs side effects	11 (31)	38 (50)	0.104	0.458 (0.197–1.065)	0.050	0.346 (0.119–1.000)
Smoking	21 (60)	23 (30)	<b>0.006</b>	3.457 (1.500–7.965)	0.139	2.136 (0.781–5.842)
Alcohol consumption	4 (11)	3 (4.9)	0.277	3.140 (0.663–14.864)	-	-
DM	17 (49)	11 (14)	<b>&lt;0.001</b>	5.581 (2.222–14.014)	<b>0.023</b>	3.444 (1.186–10.003)
Poor compliance	33 (94)	70 (92)	0.986	0.707 (0.135–3.693)	-	-
Limited access to health services	10 (29)	27 (36)	0.613	0.726 (0.304–1.734)	-	-
Bad housing condition	8 (23)	8 (11)	0.153	2.519 (0.858–7.391)	0.307	1.992 (0.530–7.484)
High housing density	10 (29)	12 (16)	0.189	2.133 (0.818–5.561)	0.779	0.832 (0.230–3.011)
Low household income	26 (74)	52 (68)	0.686	1.333 (0.543–3.277)	-	-

TB=tuberculosis; OR=odds ratio; CI=confidence interval; AFB=acid-fast bacilli; BMI=body mass index; DM=diabetes mellitus

\*Chi-square test; †binary logistic regression test, all variables that had p<0.25 using chi-square test were included in this analysis, R<sup>2</sup> = 0.465 (Nagelkerke)

## DISCUSSION

The present study found that DM and high first AFB smear grading were the predictors of smear non-conversion status among new-treatment pulmonary TB. Current study adds the evidence and strengthening previous studies<sup>2,3,8,9</sup> that concluded DM and first AFB smear grading as major predictors of smear non-conversion among new-treatment pulmonary TB. A study in Egypt concluded that delay in sputum culture conversion, moderate and extensive lung lesions, and DM were the predictors for the unsuccessful treatment of multidrug-resistant TB cases.<sup>19</sup> Hence, these findings contribute to add knowledge on some predictors of non-conversion status among new-treatment pulmonary TB in Indonesia, which previously had been limited in the hospital setting. However, the current study found no association of drug side effects, alcohol consumption, household income, and housing characteristics with smear non-conversion.

High first AFB smear grading was found playing a vital role in predicting non-conversion status with an adjusted OR of 11.22 than subjects with low smear grading. It has been reported that the first AFB smear 3+ has a higher risk of getting non-conversion after the intensive phase of treatment.<sup>20</sup> The cumulative rate of smear conversion after 2-month intensive phase of treatment for TB subjects with first AFB 2+ and 3+ was only 34%.<sup>20</sup> First AFB grading plays an important role in the management of pulmonary TB, which is describing pulmonary TB severity and transmission ability<sup>21</sup> as well as indicating the late drug resolution that related to the existence of lung cavity and the density of the Mycobacterium.

DM was found as a predictor for non-conversion among new-treatment pulmonary TB (OR = 3.44). Unfortunately, the present study did not report the glycemic control that had a meaningful impact. The present study also did not observe DM duration, severity, and chronicity that could more explain regarding treatment outcome. TB-DM optimal management is challenging. TB-DM interaction always involves issues of treatment outcome, drug-resistance, relapse, and mortality. Study reported that DM was associated with failure to sputum smear convert at 2 months and treatment failure.<sup>8</sup> Study also reported that pulmonary TB cases with DM were common to be delayed sputum conversion (prolonged positive

smear) and failure,<sup>22</sup> however, limited study reported a specific duration of treatment for TB-DM effectively. Future studies should consider these issues as well as the molecular pathways to understand underlying mechanisms and effective treatment approaches for TB-DM patients. The molecular pathways might involve advanced glycation end products and their receptors, inflammatory, oxidative stress, nuclear receptors, and cellular metabolism.<sup>8</sup>

Present study also showed that the presence of drug side effects has a higher proportion to the smear non-conversion and almost reaches the significance level ( $p = 0.05$ ). However, this condition did not match the condition of the non-compliant patient, which has a very minimum number, i.e., 6% for non-conversion status. Indeed, previous study concluded the presence of side effects implicate in treatment outcome,<sup>12</sup> but in the previous study, the observed population was the multi-drugs resistance TB, which most of them took a long period of a treatment since they were re-treatment cases.

The previous study concluded an alcohol consumption was related to the failure of TB treatment because most of them tend to default from treatment.<sup>13,16</sup> Those studies observed compliance that was closely related to default from treatment. However, the small sample size in this study limited the comprehensive analysis and understanding of their relationship. Only around 7% of the total study population were alcohol users and around 6% of the study population were non-compliant patients, without specifying how many of them were both as alcohol users and non-compliant patients. Moreover, in this study alcohol consumption status was determined for subjects that currently or former routine alcohol usage without differentiating the dosage and frequency. These conditions are certainly detailed parameters that must be observed to conclude the relationship of alcohol consumption with treatment outcomes through default from treatment as a mediation variable.

Similarly, the health care access, household income, and housing characteristics were well established as predictors of TB treatment outcome.<sup>13-16</sup> However, the present study concluded that all these predictors were not related to the smear non-conversion status. These current findings add to evidence that predictors of TB treatment outcome did not exactly the same as predictors of smear non-conversion status in



the intensive phase of treatment. Additionally, the health care access, household income, and housing characteristics could be categorized as socioeconomic determinants for treatment outcomes. Noticing these aspects, community-based study with a large sample size should be considered to conclude their associations.

Previous study reported that smoking is related to anti-tuberculosis treatment adherence.<sup>23</sup> Previous study also concluded that cigarette smoking in active pulmonary TB is related to delayed culture conversion. The frequency of delayed culture conversion after 2 months of treatment increasingly in sequentially in a group of never smokers, ex-smokers, current non-smokers, and current smokers.<sup>24</sup> This study only observed smoker status without differentiating in any detailed terms of the status.

The current study also found that the conversion rate of new-treatment pulmonary TB subjects in Dr. Kariadi General Hospital was 82.3% (209 of 254 of new-treatment pulmonary TB patients (Figure 1). This finding was in accordance with previous studies globally and Indonesia as well, which ranged from 74.7 to 90.8.<sup>3,9,10,25</sup> However, some crucial predictors, i.e., HIV/AIDS and re-treatment status that obviously will implicate the conversion rate<sup>9</sup> were excluded from this study.

The current study was conducted based on hospital data as achieving the primary goal of the study. Indeed, this study did not represent the general population condition; moreover, the status of the hospital as a national referral implies the pulmonary TB cases tend to be more complicated. This single local center study also limits generalization, therefore further study involving multi-center is needed. The use of culture to diagnose and its conversion after 2 months of treatment as well as the rapid molecular test was not observed in the present study. The most vital confounding variables, i.e., HIV/AIDS and re-treatment status, were excluded from the study implies not a comprehensive understanding of the predictors. Based on several limitations of the current study described above, further research is needed to understand the related predictors thoroughly for smear non-conversion among new-treatment pulmonary TB.

In conclusion, DM and first AFB smear grading were the predictors of smear non-conversion, suggesting that adequate attention must be considered for new-

treatment pulmonary TB subjects with DM and high AFB smear grading to achieve successful outcome treatment.

#### Conflict of Interest

The authors affirm no conflict of interest in this study.

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## REFERENCES

1. World Health Organization. Global tuberculosis report 2019 [Internet]. World Health Organization; 2019 [cited 2020 Feb]. Available from: [https://www.who.int/tb/publications/global\\_report/en/](https://www.who.int/tb/publications/global_report/en/).
2. Nandasena S, Senavirathna C, Munasinghe C, Wijesena C, Sucharitharathna R. Characteristics and sputum conversion of tuberculosis (TB) patients in Kalutara, Sri Lanka. *Indian J Tuberc*. 2019;66(1):76–80.
3. Diktanas S, Vasiliauskiene E, Polubenko K, Danila E, Celedinaite I, Boreikaite E, et al. Factors associated with persistent sputum positivity at the end of the second month of tuberculosis treatment in Lithuania. *Tuberc Respir Dis (Seoul)*. 2018;81(3):233–40.
4. Kayigamba FR, Bakker MI, Mugisha V, De Naeyer L, Gasana M, Cobelens F, et al. Adherence to tuberculosis treatment, sputum smear conversion and mortality: a retrospective cohort study in 48 Rwandan clinics. *PLoS One*. 2013;8(9):e73501.
5. D'Souza KA, Zaidi SMA, Jaswal M, Butt S, Khowaja S, Habib SS, et al. Factors associated with month 2 smear non-conversion among category 1 tuberculosis patients in Karachi, Pakistan. *J Infect Public Health*. 2018;11(2):283–5.
6. Lee SH, Seo KA, Lee YM, Lee HK, Kim JH, Shin C, et al. Low serum concentrations of moxifloxacin, prothionamide, and cycloserine on sputum conversion in multi-drug resistant TB. *Yonsei Med J*. 2015;56(4):961–7.
7. Masjedi MR, Hosseini M, Aryanpur M, Mortaz E, Tabarsi P, Soori H, et al. The effects of smoking on treatment outcome in patients newly diagnosed with pulmonary tuberculosis. *Int J Tuberc Lung Dis*. 2017;21(3):351–6.
8. Critchley JA, Restrepo BI, Ronacher K, Kapur A, Bremer AA, Schlesinger LS, et al. Defining a research agenda to address the converging epidemics of tuberculosis and diabetes: part 1: epidemiology and clinical management. *Chest*. 2017;152(1):165–73.
9. Mlotshwa M, Abraham N, Beery M, Williams S, Smit S, Uys M, et al. Risk factors for tuberculosis smear non-conversion in Eden district, Western Cape, South Africa, 2007–2013: a retrospective cohort study. *BMC Infect Dis*. 2016;16:365.
10. Tama TD, Adisasmita AC, Burhan E. Body mass index and time to sputum smear conversion among acid-fast bacilli (AFB) positive pulmonary tuberculosis patients at RSUP Persahabatan 2012. *J Epidemiol Kesehat Indones*. 2016;1(1):1–8. Indonesian.
11. Bineni C, Yarasani P, Ravi Prabhu G. A study on role of sputum conversion rate in management of tuberculosis in South Indian population. *Int J Community Med Public Health*. 2018;5(4):1419–23.
12. Piparva KG, Jansari G, Singh AP. Evaluation of treatment outcome and adverse drug reaction of directly observed treatment (DOT) plus regimen in multidrug-resistant tuberculosis (MDR-TB)

- patients at district tuberculosis centre Rajkot. *Perspect Clin Res*. 2018;9(4):165–9.
13. Muture BN, Keraka MN, Kimuu PK, Kabiru EW, Ombeka VO, Oguya F. Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: a case control study. *BMC Public Health*. 2011;11:696.
  14. Dangisso MH, Datiko DG, Lindtjørn B. Accessibility to tuberculosis control services and tuberculosis programme performance in southern Ethiopia. *Glob Health Action*. 2015;8:29443.
  15. Low CT, Lai PC, Tse WSC, Tsui CK, Lee H, Hui PK. Exploring tuberculosis by types of housing development. *Soc Sci Med*. 2013;87:77–83.
  16. Peltzer K, Louw JS. Prevalence and factors associated with tuberculosis treatment outcome among hazardous or harmful alcohol users in public primary health care in South Africa. *Afr Health Sci*. 2014;14(1):157–66.
  17. Maciel EL, Brioschi AP, Peres RL, Guidoni LM, Ribeiro FK, Hadad DJ, et al. Smoking and 2-month culture conversion during anti-tuberculosis treatment. *Int J Tuberc Lung Dis*. 2013;17(2):225–8.
  18. Lemeshow S, Hosmer DW Jr, Klar J, Lwanga SK. Adequacy of sample size in health studies. World Health Organization; 1990.
  19. Gadallah MA, Mokhtar A, Rady M, El-Moghazy E, Fawzy M, Kandil SK. Prognostic factors of treatment among patients with multidrug-resistant tuberculosis in Egypt. *J Formos Med Assoc*. 2016;115(11):997–1003.
  20. Jayakody W, Harries AD, Malhotra S, de Alwis S, Samaraweera S, Pallewatta N. Characteristics and outcomes of tuberculosis patients who fail to smear convert at two months in Sri Lanka. *Public Health Action*. 2013;3(1):26–30.
  21. Nwokeukwu HI, Awujo D, Emma-Ukeagbu U. Association of sputum conversion and outcome with initial smear grading among new smear positive tuberculosis patients in a Tertiary Health Facility, South East Zone, Nigeria. *IOSR J Dent Med Sci*. 2013;4(6):21–5.
  22. Viswanathan V, Vigneswari A, Selvan K, Satyavani K, Rajeswari R, Kapur A. Effect of diabetes on treatment outcome of smear-positive pulmonary tuberculosis—a report from South India. *J Diabetes Complications*. 2014;28(2):162–5.
  23. Underner M, Perriot J, Peiffer G, Meurice JC, Dautzenberg B. Smoking and adherence to anti-tuberculosis treatment Smoking and adherence to anti-tuberculosis treatment. *Rev Mal Respir*. 2016;33(2):128–44.
  24. Nijenbandring de Boer R, Oliveira e Souza Filho JB, Cobelens F, Ramalho Dde P, Campino Miranda PF, Logo KD, et al. Delayed culture conversion due to cigarette smoking in active pulmonary tuberculosis patients. *Tuberculosis*. 2014;94(1):87–91.
  25. Saffari M, Jolandimi HA, Sehat M, Nejad NV, Hedayati M, Zamani M, et al. Smear grading and the Mantoux skin test can be used to predict sputum smear conversion in patients suffering from tuberculosis. *GMS Hyg Infect Control*. 2017;12:Doc12.