Homa Serpoosh[1, 2], **Yadollah Hamidi**[1], **Payman Eini**[3], **Younes Mohammadi**[4, 5]

[1]Department of Health Economy and Management, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran
[2]Students Research Committee, Hamadan University of Medical Sciences, Hamadan, Iran
[3]Department of Infectious Disease, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[4]Social Determinants of Health Research Center, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran
[5]Department of Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

Association of smoking and drug abuse with treatment failure in individuals with tuberculosis: a case-control study

Abstract

Introduction: Treatment failure in tuberculosis (defined as a positive sputum smear 5 months after the initiation of anti-TB treatment) is a major threat to the control over TB. This study aimed to investigate the association of smoking and drug abuse with treatment failure among individuals with TB.

Material and methods: Out of 286 TB patients with available data registered by the health system of Hamadan Provinces in western Iran, 24 TB patients with treatment failure (positive sputum smear, 5 months after initiation of anti-TB treatment) and 262 patients without treatment failure (negative sputum smear, five months after initiation of anti-TB treatment) were selected as case and control groups, respectively. These two groups were compared to each other in terms of demographic status which include age, sex, job, residence, and risk factors such as smoking and drug abuse status. An odds ratio (OR) with a 95% confidence interval was used as a measure of association. The Bonferroni correction was used to counteract multiple comparisons, therefore, a p-value of less than 0.004 was statistically significant.

Results: No significant association was found between treatment failure and age, residence, comorbidity, education level, job status, sex, smoking, and method of drug abuse (P > 0.004). However, a significant association was found between duration of smoking, number of cigarettes per day, and drug abuse with treatment failure in univariate analysis (P < 0.004). In multivariate analysis, only an association with drug abuse was significantly associated with treatment failure (P = 0.047).

Conclusion: Drug abuse substantially increases the risk of treatment failure. Therefore, in order to control TB, it is suggested that preventive programs are designed in order to decrease drug abuse among TB patients before starting treatment.

Key words: tuberculosis, smoking, drug abuse, treatment outcome

Adv Respir Med. 2020; 88: 383–388

Introduction

Tuberculosis (TB) is a contagious and airborne disease caused mainly by Mycobacterium tuberculosis, but also rarely by Mycobacterium bovis and africanum [1]. Many of the health and medical interventions used to control TB have resulted in a remarkable reduction of the disease over recent decades [2]. Despite this substantial progress against TB, it has remained as one of ten major causes of death in the world. Based on the global tuberculosis report of 2018 conducted by the World Health Organization (WHO), 10 million people developed TB disease and 1.3 million people died from TB [3, 4]. In addition, the report reveals that 90% of cases of TB and deaths due to the disease occur in developing countries [5]. Moreover, the studies report that nearly one-third of the world's population is infected with tuberculosis [6, 7].

Many risk factors have been identified that increase the risk of developing TB. Poverty, HIV infection, substance abuse, alcohol consumption, silicosis, diabetes mellitus, severe kidney disease,

low body weight, organ transplants, and head and neck cancers are examples of risk factors that are confirmed to increase the risk of being infected with TB [8–11]. Therefore, preventing and removing these risk factors may decrease the prevalence of TB remarkably.

The WHO's recommended strategy for controlling TB is via treatment of patients using the DOTS (Directly Observed Treatment, Short-course) program [12]. As the WHO claims, "the most cost-effective way to stop the spread of TB in communities with a high incidence is by curing it" [13]. This strategy has five elements that include government commitment, case detection, treatment regimen, standardized recording, and a structured reporting system. The major threat to this strategy is treatment failure of TB [14]. Treatment failure occurs in patients who, five months after initiation of anti-TB treatment, have positive sputum smears [15]. Treatment failure increases the probability of drug resistance and may result in the spread of TB. Several factors contribute to treatment failure such as age, sex, education level, alcohol consumption, HIV, and weight loss [16-19]. Another two suspected risk factors that may have a role in treatment failure are smoking and drug abuse. However, findings on these two risk factors are not clarified well, and results are contradictory. While some studies confirm existence of an association between smoking and drug abuse with treatment [20], other studies did not endorse such an association [21]. Reaching a consensus on this issue requires more research. Therefore, in this study, we aimed to investigate the identity and existence of this association between smoking and drug abuse with treatment failure of TB in Hamadan province, western Iran.

Material and methods

Type of study

This study was a case-control study.

Setting and population

The study was conducted in Hamadan province, western Iran. The study population included all patients with confirmed tuberculosis who were registered by the health system of the province from 2010 to 2018 and who underwent anti-TB treatment. Based on the Iranian national guidelines for the control of TB, sputum smear microscopy (SSM) was used to diagnose TB in patients.

After confirmation of TB in individuals, they underwent directly observed treatment based on the short-course (DOTS) program. However, if positive sputum smear results remained 5 months after the initiation of treatment, the result was labelled treatment failure. Accordingly, in this case-control study, we defined the case group (with treatment failure) as TB patients who, five months after initiation of anti-TB treatment, had positive sputum smear results. On the other hand, we defined the control group as TB patients who, 5 months after initiation of anti-TB treatment, had negative sputum smears. In the case that the patients died before completion of treatment course, or if there was no available data, they were excluded from the study. Accordingly, out of 321 patients registered by the system, 24 had treatment failure (case) and 262 patients were without treatment failure (control) and with available data included in the study. Thirty-five patients were excluded from the study because there was no data available for them.

Variables

According to data registered by the system, variables of this study included age, sex, education level, job, residence, comorbidity, family history of TB, smoking status, number of cigarettes per day, duration of smoking, drug abuse status, and type of drug abuse. For this study, we defined a "smoker" as an individual who smokes at least one cigarette every day.

Statistical analysis

We used bivariate analysis including ANOVA and the chi-square test to assess the difference between case and control groups. Moreover, we used logistic regression to adjust the confounding effect of other variables. An odds ratio with a 95% confidence interval was used as a measure of association. Further, in order to deal with multiple comparison problems in the tests, we used the Bonferroni correction to adjust the p-value. Therefore, a p-value less than 0.004 was statistically significant. The Hosmer and Lemeshow test was used to verify goodness of fit for the regression model.

Ethical considerations

The study has been registered by the Ethics Committee of Hamadan University of Medical Sciences (NO. IR.UMSHA.REC.1397.498). Furthermore, all information collected was considered as confidential.

Results

Out of the 321 registered patients who underwent anti-TB treatment, data for 286 patients

was available. Five months after initiation of anti-TB treatment, sputum results were positive for 24 patients and negative for 262 patients (control group). Out of 35 patients that were without data for analysis, 28 patients (80%) died before completion of the treatment course. Moreover, data for the outcome of seven patients was not retrievable.

Table 1 demonstrates the demographic and risk factor characteristics for the case and control groups. As shown in the table, despite 75% of the case group and 48.5% of the control group being men, the p-value, according to the Bonferroni correction, was less than 0.01. Therefore, sex difference between case and control group was not statistically significant at a level of 0.004. Moreover, we did not find a significant

difference between two groups in terms of age, education, job, residence, family history of TB, and co-morbidity (p > 0.004).

In terms of smoking, results presented in table 1 showed that the percentage of smokers in case groups is substantially higher than in the control group (58% *vs* 35%). In other words, the odds of patients being smokers was 2.58 times higher in the case group than in the control group. However, this difference was not statistically significant at a level p > 0.004. The duration of smoking was significantly associated with treatment failure (p = 0.001). Moreover, patients in the case group smoked on average eight cigarettes per day more than patients in the control group (p < 0.001). In terms of duration of smoking, the mean duration of smoking in the case group

Table 1. Demographic and risk factor description in case and control groups

	Case (n = 24)	Control (n = 262)	
Mean (SD) age [year]	54 ± 20.9	53.6 ± 20.6	ANOVA [F (1,284) = 0.008, p = 0.93)]
Mean (SD) duration of smoking [year]	17.7 ± 14.3	9.4 ± 13.3	ANOVA [F (1,284) = 8.54, p = 0.004)]
Mean (SD) cigarettes smoked per day [number]	14.7 ± 11.4	6.4 ± 9.4	ANOVA [F (1,276) = 15.86, p = < 0.001)]
Male	18 (75%)	127 (48.5%)	0.01
Education level			
Illiterate	5 (20.7%)	71 (27.1%)	
Primary	4 (16.7%)	55 (21%)	
Guidance school	10 (41.7%)	70 (26.7%)	0.33
High school	1 (4.2%)	38 (14.5%)	
Diploma and more	4 (16.7%)	28 (10.7%)	
Urban	16 (66.7%)	167 (63.7%)	
Job status			
Employee	2 (8.3%)	29 (11.1%)	
Worker	0 (0%)	28 (3.1%)	
Housewife	5 (20.8%)	105 (40 %)	
Freelance	9 (37.5%)	55 (21%)	0.17
Unemployed	3 (12.5%)	6 (2.3%)	
Student	1 (4.2%)	12 (4.5%)	
Other	4 (16.7%)	47 (18%)	
Family history of TB	5 (20.8%)	64 (24.5%)	0.95
Comorbidity	6 (25%)	55 (21%)	0.16
Smoker	14 (58.3%)	92 (35%)	0.02
Drug abuser	11 (45.8%)	57 (21.8%)	0.001
Drug abuse method			
Swallowing	1 (7.3%)	21 (37.6%)	
Injection	8 (57%)	12 (21.4%)	0.32
Inhalation	5 (35.7%)	23 (41%)	

low body weight, organ transplants, and head and neck cancers are examples of risk factors that are confirmed to increase the risk of being infected with TB [8–11]. Therefore, preventing and removing these risk factors may decrease the prevalence of TB remarkably.

The WHO's recommended strategy for controlling TB is via treatment of patients using the DOTS (Directly Observed Treatment, Short-course) program [12]. As the WHO claims, "the most cost-effective way to stop the spread of TB in communities with a high incidence is by curing it" [13]. This strategy has five elements that include government commitment, case detection, treatment regimen, standardized recording, and a structured reporting system. The major threat to this strategy is treatment failure of TB [14]. Treatment failure occurs in patients who, five months after initiation of anti-TB treatment, have positive sputum smears [15]. Treatment failure increases the probability of drug resistance and may result in the spread of TB. Several factors contribute to treatment failure such as age, sex, education level, alcohol consumption, HIV, and weight loss [16-19]. Another two suspected risk factors that may have a role in treatment failure are smoking and drug abuse. However, findings on these two risk factors are not clarified well, and results are contradictory. While some studies confirm existence of an association between smoking and drug abuse with treatment [20], other studies did not endorse such an association [21]. Reaching a consensus on this issue requires more research. Therefore, in this study, we aimed to investigate the identity and existence of this association between smoking and drug abuse with treatment failure of TB in Hamadan province, western Iran.

Material and methods

Type of study
This study was a case-control study.

Setting and population
The study was conducted in Hamadan province, western Iran. The study population included all patients with confirmed tuberculosis who were registered by the health system of the province from 2010 to 2018 and who underwent anti-TB treatment. Based on the Iranian national guidelines for the control of TB, sputum smear microscopy (SSM) was used to diagnose TB in patients.

After confirmation of TB in individuals, they underwent directly observed treatment based on the short-course (DOTS) program. However, if

positive sputum smear results remained 5 months after the initiation of treatment, the result was labelled treatment failure. Accordingly, in this case-control study, we defined the case group (with treatment failure) as TB patients who, five months after initiation of anti-TB treatment, had positive sputum smear results. On the other hand, we defined the control group as TB patients who, 5 months after initiation of anti-TB treatment, had negative sputum smears. In the case that the patients died before completion of treatment course, or if there was no available data, they were excluded from the study. Accordingly, out of 321 patients registered by the system, 24 had treatment failure (case) and 262 patients were without treatment failure (control) and with available data included in the study. Thirty-five patients were excluded from the study because there was no data available for them.

Variables
According to data registered by the system, variables of this study included age, sex, education level, job, residence, comorbidity, family history of TB, smoking status, number of cigarettes per day, duration of smoking, drug abuse status, and type of drug abuse. For this study, we defined a "smoker" as an individual who smokes at least one cigarette every day.

Statistical analysis
We used bivariate analysis including ANOVA and the chi-square test to assess the difference between case and control groups. Moreover, we used logistic regression to adjust the confounding effect of other variables. An odds ratio with a 95% confidence interval was used as a measure of association. Further, in order to deal with multiple comparison problems in the tests, we used the Bonferroni correction to adjust the p-value. Therefore, a p-value less than 0.004 was statistically significant. The Hosmer and Lemeshow test was used to verify goodness of fit for the regression model.

Ethical considerations
The study has been registered by the Ethics Committee of Hamadan University of Medical Sciences (NO. IR.UMSHA.REC.1397.498). Furthermore, all information collected was considered as confidential.

Results

Out of the 321 registered patients who underwent anti-TB treatment, data for 286 patients

Table 2. Logistic regression analyses of factors associated with treatment failure in TB patients

Variable	Crude odds ratio (95% CI)	p-value	Adjusted odds ratio (95%CI)	p-value
Age	1 (0.98,1.02)	0.93	1 (0.98–1.02)	0.79
Sex	3.2 (1.22,8.2)	0.02	1.55 (0.45–5.31)	0.48
Smoker	2.58 (1.1, 6.1)	0.02	1.26 (0.42–3.76)	0.67
Drug abuser	4.2 (1.8, 9.95)	0.001	2.98 (1.02–7.14)	0.047
Constant	—	—	1.210	0.84

was eight years longer than in the control group, which was statistically significant (p = 0.004).

In terms of drug abuse status, as demonstrated In table 1, we found that 46% of patients in the case group and 22% in the control group were drug abusers. Therefore, drug abusers were 4 times more likely to have treatment failure (p < 0.001). However, when investigating the method of drug abuse between the two groups, the method of abuse did not result in a significant difference (p = 0.32).

To adjust for the confounding effect of the variables, we used logistic regression. As shown in Table 2, only drug abuse is significantly associated with treatment failure in TB patients, with a 3 times greater likelihood that failure occurs (p = 0.047). The result of the Hosmer and Lemeshow test for goodness of fit for logistic regression models was not significant, which means that the model is a good fit (Chi-square = 3.08, df = 8, p = 0.93).

Discussion

In this study, we aimed to explore the association of smoking and drug abuse with treatment failure in TB patients (defined as a positive sputum smear five months after the initiation of treatment). Our study showed that drug abuse was significantly associated with treatment failure. Although the failure rate among smokers and drug abusers was higher than non-smokers and drug abusers, after adjusting for the effects of other factors, only the effect of drug abuse remained as significant (increasing the risk of treatment failure by 3.5 times). This result reveals the major effect of drug abuse on treatment failure. Although we did not observe a significant association between smoking and treatment failure in multivariate analysis, it seems that this association exists. The most important reason for a lack of association between smoking and treatment failure in our study was our small sample size (low power of

study). However, there is significant evidence for this association being present in our study. In this study, we investigated the association between the number of cigarettes smoked per day and duration of smoking with treatment failure. We found that a significant association exists between them seeing as the number of cigarettes per day and duration of smoking was substantially higher in patients with treatment failure than patients without treatment failure. In epidemiology, this issue is called "dose–response relationship" [22], which is one of the major criteria for a causal association to be made between an exposure and an outcome of interest. In addition, given that data for smoking and drug abuse was collected before the initiation of treatment, another criterion of causality which is called "temporality" is likely established [22]. This criterion is the most important factor for establishing causality in epidemiology. Another criterion for establishing causality is identifying a consistency of findings [22]. The majority of previous studies confirmed our results. In a cohort study in Peru, it was found that both smoking and drug abuse were significantly associated with treatment failure, and that the effect of drug abuse was stronger than the effect of smoking. The paper recommended identifying smokers and drug abusers before initiating treatment to increase the probability of treatment success of TB [23]. In addition, in a study conducted in Brazil aimed to examine the role of drug abuse as a predictor of treatment failure, it was reported that 33% of drug abusers and 7% of non-drug abusers had treatment failure. Our study had similar results showing that about 34.8% of smokers and 12.5% of non-smokers had treatment failure [24]. However, some studies did not find a significant association between smoking and drug abuse with treatment failure. For example, El-Shabrawy *et al* found that, despite a high rate of treatment failure in smokers compared with non-smokers, no significant association between smoking and treatment failure

existed [21]. Apparently, a small sample size of their study was the main reason for this result. Further, Alo in Fiji did not observe a significant association between smoking status and treatment failure [25]. However, despite these contradictory results, the existence of an association is likely. To properly explain these differing results, we recommend performing a meta-analysis since there is evidence indicating that there is an association between drug abuse and smoking with treatment failure.

With consideration to the association between smoking and drug abuse with treatment failure and the global prevalence of smoking (20%) and drug abuse (2%) in the world [26–28], especially in low and middle-income countries where the prevalence of TB is high, it will be very difficult to control the spread of TB [29]. Many studies show that the prevalence of smoking and drug abuse among TB patients is a critical aspect of disease control. In a study by Burnet, the estimated prevalence of smoking in patients with active and latent infection was 56% and 60%, respectively[30]. Therefore, this high prevalence of smoking in TB patients results in treatment failure and eventually, death. In addition, failure to properly control TB increases the spread of TB in the population. It is also important to note the role of drug abuse and the AIDS epidemic as important factors in the spread of TB [31, 32].

Literature explains the mechanisms of how smoking and drug abuse affect treatment failure. It seems that two likely pathways exist for how smoking and drug abuse influence the treatment outcome. The studies reveal that an interaction of TB with smoking and drug abuse exists at a cellular level and may result in a decreased level of immunity through reduction in activity of macrophages, dendritic cells, and natural killer cells [33]. Moreover, studies demonstrated that smoking and drug abuse are associated with a low adherence to treatment in male TB patients [34].

This study has two messages to policy-makers: Firstly, statistics regarding the high amount of patients with treatment failure in TB is remarkable. As noted before, treatment failure is the biggest threat for the control of TB and, as such, paying special attention to treatment failure is necessary. Secondly, smoking and drug abuse showed a significant effect on treatment failure, and this has been reciprocated by many other studies which also confirm this issue. Therefore, it is recommended to design programs for the cessation of smoking and drug abuse before initiating treatment of TB.

This study has limitations. Firstly, sample size, especially in our case group, is small. Small sample size may reduce the power of study to detect significant differences. This issue is one of the determinants for a non-significant association between smoking and treatment failure. Secondly, we used data registered by the TB system which is known to have problems in accuracy and in incomplete registrations. Thirdly, we could not obtain some important information such as percentage of multidrug resistance and HIV disease status among TB patients. This information may present a more clarified picture of the TB patients we studied. Fourthly, a number of the patients died or were lost to follow up before completion of the treatment course. Therefore, we performed our analysis only on patients who survived, which may have led to selection bias affecting our final result. Based on these limitations, designing a prospective cohort with an accurate registration of information and with interventional studies to assess the effectiveness of smoking and drug abuse cessation programs on treatment failure is recommended.

Conclusion

Our results confirm that drug abuse is associated with treatment failure in TB patients. However, smoking significantly increased the risk of treatment failure as well. Therefore, it suggested that cessation of smoking and drug abuse accompany the initiation of treatment programs for TB patients. Training health workers to be able to detect smokers and drug abusers should also be incorporated into treatment programs to increase the efficacy of TB treatment.

Acknowledgment

Conflict of interest

The authors have no conflict of interest.

References:

1. Gagneux S. Ecology and evolution of mycobacterium tuberculosis. Nat Rev Microbiol. 2018; 16(4): 202–213, doi: 10.1038/nrmicro.2018.8, indexed in Pubmed: 29456241.
2. MacNeil A, Glaziou P, Sismanidis C, et al. Global epidemiology of tuberculosis and progress toward achieving global targets 2017. MMWR Morb Mortal Wkly Rep. 2019; 68(11): 263–266, doi: 10.15585/mmwr.mm6811a3, indexed in Pubmed: 30897077.

3. Dirlikov E, Raviglione M, Scano F. Global tuberculosis control: toward the 2015 targets and beyond. Ann Intern Med. 2015; 163(1): 52–58, doi: 10.7326/M14-2210, indexed in Pubmed: 25915859.
4. World Health Orgnization. Global Tuberculosis Report 2019, 2018.
5. Getahun H, Matteelli A, Abubakar I, et al. Latent mycobacterium tuberculosis infection. N Engl J Med. 2015; 372(22): 2127–2135, doi: 10.1056/NEJMra1405427, indexed in Pubmed: 26017823.
6. Cohen A, Mathiasen VD, Schön T, et al. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. Eur Respir J. 2019; 54(3), doi: 10.1183/13993003.00655-2019, indexed in Pubmed: 31221810.
7. Houben RM, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. PLoS Med. 2016; 13(10): e1002152, doi: 10.1371/journal.pmed.1002152, indexed in Pubmed: 27780211.
8. Mahara G, Yang K, Chen S, et al. Socio-Economic predictors and distribution of tuberculosis incidence in Beijing, China: a study using a combination of spatial statistics and GIS technology. Med Sci (Basel). 2018; 6(2), doi: 10.3390/medsci6020026, indexed in Pubmed: 29561814.
9. Imtiaz S, Shield KD, Roerecke M, et al. Alcohol consumption as a risk factor for tuberculosis: meta-analyses and burden of disease. Eur Respir J. 2017; 50(1), doi: 10.1183/13993003.00216-2017, indexed in Pubmed: 28705945.
10. Silva DR, Muñoz-Torrico M, Duarte R, et al. Risk factors for tuberculosis: diabetes, smoking, alcohol use, and the use of other drugs. J Bras Pneumol. 2018; 44(2): 145–152, doi: 10.1590/s1806-37562017000000443, indexed in Pubmed: 29791552.
11. Narasimhan P, Wood J, Macintyre CR, et al. Risk factors for tuberculosis. Pulm Med. 2013; 2013: 828939, doi: 10.1155/2013/828939, indexed in Pubmed: 23476764.
12. Gebrezgabiher G, Romha G, Ejeta E, et al. Treatment outcome of tuberculosis patients under directly observed treatment short course and factors affecting outcome in Southern Ethiopia: a five-year retrospective study. PLoS One. 2016; 11(2): e0150560, doi: 10.1371/journal.pone.0150560, indexed in Pubmed: 26918458.
13. World Health Organization. Tuberculosis control: the DOTS strategy (Directly Observed Treatment Short-Course): an annotated bibliography. World Health Organization, 1997.
14. Gandhi NR, Nunn P, Dheda K, et al. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. Lancet. 2010; 375(9728): 1830–1843, doi: 10.1016/S0140-6736(10)60410-2, indexed in Pubmed: 20488523.
15. Cherkaoui I, Sabouni R, Ghali I, et al. Risk factors for tuberculosis treatment failure, default, or relapse and outcomes of retreatment in Morocco. BMC Public Health. 2011; 11(4): 140, doi: 10.1186/1471-2458-11-140, indexed in Pubmed: 21356062.
16. Diallo A, Dahourou DL, Dah TT, et al. Factors associated with tuberculosis treatment failure in the Central East Health region of Burkina Faso. Pan Afr Med J. 2018; 30: 293, doi: 10.11604/pamj.2018.30.293.15074, indexed in Pubmed: 30637077.
17. Diallo A, Dahourou DL, Dah TT, et al. Factors associated with tuberculosis treatment failure in the Central East Health region of Burkina Faso. Pan Afr Med J. 2018; 30: 293, doi: 10.11604/pamj.2018.30.293.15074, indexed in Pubmed: 30637077.
18. Pizzol D, Veronese N, Marotta C, et al. Predictors of therapy failure in newly diagnosed pulmonary tuberculosis cases in Beira, Mozambique. BMC Res Notes. 2018; 11(1): 99, doi: 10.1186/s13104-018-3209-9, indexed in Pubmed: 29402317.
19. Namukwaya E, Nakwagala FN, Mulekya F, et al. Predictors of treatment failure among pulmonary tuberculosis patients in Mulago hospital, Uganda. Afr Health Sci. 2011; 11 Suppl 1: S105–S111, doi: 10.4314/ahs.v11i3.70079, indexed in Pubmed: 22135634.
20. Lackey B, Seas C, Van der Stuyft P, et al. Patient characteristics associated with tuberculosis treatment default: a cohort study in a high-incidence area of Lima, Peru. PLoS One. 2015; 10(6): e0128541, doi: 10.1371/journal.pone.0128541, indexed in Pubmed: 26046766.
21. El-Shabrawy M, El-Shafei D. Evaluation of treatment failure outcome and its predictors among pulmonary tuberculosis patients in Sharkia Governorate, 2013–2014. Egyptian Journal of Chest Diseases and Tuberculosis. 2017; 66(1): 145–152, doi: 10.1016/j.ejcdt.2015.11.002.
22. Greenland S, Lash TL. Rothman KJ, Greenland S, Lash TL. Modern epidemiology. Lippincott Williams & Wilkins 2008.
23. Lackey B, Seas C, Van der Stuyft P, et al. Patient characteristics associated with tuberculosis treatment default: a cohort study in a high-incidence area of Lima, Peru. PLoS One. 2015; 10(6): e0128541, doi: 10.1371/journal.pone.0128541, indexed in Pubmed: 26046766.
24. Silva MR, Pereira JC, Costa RR, et al. Drug addiction and alcoholism as predictors for tuberculosis treatment default in Brazil: a prospective cohort study. Epidemiol Infect. 2017; 145(16): 3516–3524, doi: 10.1017/S0950268817002631, indexed in Pubmed: 29173226.
25. Alo A, Gounder S, Graham SM. Clinical characteristics and treatment outcomes of tuberculosis cases hospitalised in the intensive phase in Fiji. Public Health Action. 2014; 4(3): 164–168, doi: 10.5588/pha.14.0022, indexed in Pubmed: 26400804.
26. Bashirian S, Barati M, Mohammadi Y, et al. Factors associated with hookah use among male high school students: the role of demographic characteristics and hookah user and non-user prototypes. J Res Health Sci. 2016; 16(4): 217–223, indexed in Pubmed: 28087855.
27. Organization WH. WHO global report on trends in prevalence of tobacco smoking 2000-2025: World Health Organization; 2018.
28. Peacock A, Leung J, Larney S, et al. Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. Addiction. 2018; 113(10): 1905–1926, doi: 10.1111/add.14234, indexed in Pubmed: 29749059.
29. World Health Organization. Smoking and tuberculosis: a dangerous combination 2018 [cited 2020]. Available from: http://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/news/news/2018/3/smoking-and-tuberculosis-a-dangerous-combination. [Last accessed: 04.09.2020].
30. Brunet L, Pai M, Davids V, et al. High prevalence of smoking among patients with suspected tuberculosis in South Africa. Eur Respir J. 2011; 38(1): 139–146, doi: 10.1183/09031936.00137710, indexed in Pubmed: 21148230.
31. Deiss RG, Rodwell TC, Garfein RS. Tuberculosis and illicit drug use: review and update. Clin Infect Dis. 2009; 48(1): 72–82, doi: 10.1086/594126, indexed in Pubmed: 19046064.
32. Getahun H, Baddeley A, Raviglione M. Managing tuberculosis in people who use and inject illicit drugs. Bull World Health Organ. 2013; 91(2): 154–156, doi: 10.2471/BLT.13.117267, indexed in Pubmed: 23554532.
33. Schneider NK, Novotny TE. Addressing smoking cessation in tuberculosis control. Bull World Health Organ. 2007; 85(10): 820–821, doi: 10.2471/blt.07.034797, indexed in Pubmed: 18038065.
34. Adane AA, Alene KA, Koye DN, et al. Non-adherence to anti-tuberculosis treatment and determinant factors among patients with tuberculosis in northwest Ethiopia. PLoS One. 2013; 8(11): e78791, doi: 10.1371/journal.pone.0078791, indexed in Pubmed: 24244364.