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Original Article

Factors affecting successful treatment outcomes in pulmonary tuberculosis: a single-center experience in Turkey, 2005–2011

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Abstract

Introduction: We aimed to describe the treatment outcomes in patients with bacteriologically confirmed pulmonary tuberculosis (PTB) and identify factors associated with successful treatment outcome.

Methodology: The medical charts of patients with smear and/or culture-positive PTB who were treated between 2005 and 2011 at the Kocaeli Tuberculosis Dispensary, Turkey, were reviewed. Patients were categorized as having a successful (cured or with a completed treatment) or poor (treatment default, treatment failure, death) treatment outcome. The association of demographic and clinical factors, including gender, age, education, occupation, insurance, family size, living area, smear and culture positivity, retreatment, comorbidity, drug resistance, and cavity on radiography, with the success of treatment, was evaluated by univariate and multivariate analyses.

Results: Of 738 patients (258 females, 480 males) with bacteriologically confirmed PTB, 683 (92.6%) had successful treatment outcomes. Of those with a poor outcome, 29 (3.9%) had treatment default, 18 (2.4%) died, and 8 (1.1%) had treatment failure. Young age, no previous treatment, no comorbidity, no drug resistance, and high education level were factors significantly associated with successful PTB treatment outcome ($p < 0.05$ for all).

Conclusions: Treatment outcome was successful in young and educated PTB patients who had drug resistance, previous treatment history, and no comorbidities. Knowledge of the factors affecting treatment success will lead to the undertaking of specific measures in the management of PTB, which may help to decrease treatment failure.

Key words: pulmonary tuberculosis; treatment outcome; drug resistance; Turkey.

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Introduction

Tuberculosis (TB) remains a serious public health problem across the world. In 2012, there were an estimated 12 million TB cases, with 8.6 million new cases and 1.3 million fatal cases all worldwide. A global TB strategy was initiated in the 1990s with increased use of directly observed treatment, short-course (DOTS). The diagnostic and therapeutic implementations based on the DOTS/Stop TB Strategy have led to significant success in the control of TB. The main objective of the Stop TB Strategy is to dramatically reduce the global burden of tuberculosis by 2015. Between 1995 and 2012, 56 million people were successfully treated for TB in countries that had adopted the global TB strategy, which saved 22 million lives [1,2].

The Stop TB Strategy was launched in 2006. Turkey also committed to implementing the Stop TB Strategy within the context of the Berlin Declaration on Tuberculosis, which included recommendations by the World Health Organization (WHO) and was adopted by all countries in 2007, and it initiated strategic requirements [3]. The treatment and follow-up of patients with tuberculosis are carried out according to the WHO guidelines, and are provided free of charge by TB dispensaries in Turkey, where there is at least one dispensary in each province.

The point prevalence of tuberculosis in Turkey, which was 52 per 100,000 in 1990, was reduced to 23 per 100,000 in 2012, achieving the target prevalence [3-5]. A WHO report indicated that the estimated case detection rate was 87% in 2012, and the treatment

success rate was 90% in patients with new bacteriologically confirmed pulmonary tuberculosis in 2011 in Turkey [5].

Kocaeli is an industrial city with a population of 1.6 million and a high gross domestic product (GDP) per capita. According to the data from the Kocaeli Tuberculosis Dispensary, the treatment success rate was 91.6% when all tuberculosis cases were considered between 2005 and 2011, and almost all of the patients received directly observed treatment (DOT) according to the 2009 data [4]. One of the main components of the final target of WHO to eliminate TB is the increase of the treatment success rate to the highest level. For this purpose, being familiar with the factors affecting the treatment failure and developing specific treatment strategies for these patient groups may contribute to the success in the fight against TB. Demonstrating the effect of sociocultural and economic differences specific to each country or region will increase the awareness of healthcare professionals and increase treatment success. Based on this, we aimed to evaluate treatment outcomes in patients with bacteriologically confirmed pulmonary tuberculosis and factors affecting treatment success in our region.

Methodology

The present study was carried out in Kocaeli, in the northwest of Turkey. It was conducted as a retrospective cohort study. The medical charts of the patients with smear and/or culture positive pulmonary tuberculosis who were treated between 2005 and 2011 at the Kocaeli Tuberculosis Dispensary were reviewed. Patients who transferred out, who were younger than 15 years of age, whose medical charts were not obtained, and multidrug-resistant (MDR) patients who received a second-line therapy, were excluded.

Outcome definition

Treatment success and poor outcome were defined according to the WHO criteria.

Successful treatment outcome was defined as follows.

a. Cured: A clinical and radiological improvement in a patient with a baseline smear positivity and evidence of at least two negative sputum smears, one during the maintenance period, and the other when the treatment was completed.
b. Completed treatment: Completion of treatment during the predicted treatment period in patients with clinical and radiological improvement.

Unsuccessful outcome was defined as follows.

c. Treatment failure: Detection of positive sputum smear in a patient at month five or later during the treatment.
d. Default: A patient who did not receive his/her medications for two months or more.
e. Death: A patient who died of tuberculosis or for any other reason during the course of treatment.

Another outcome, "Not evaluated"', was used for patients whose treatment outcome was unknown, including transfers out. This group was not included in the present study [1].

A new case was defined as a patient who had never had treatment for TB or had taken treatment for less than one month, while a retreatment case was defined as a patient who had previously taken treatment for more than one month (relapse, treatment after failure, and treatment after default) [1].

New cases received isoniazid (H), rifampicin (R), ethambutol (E), and pyrazinamide (Z) for two months, and a standard short-course treatment as HR treatment for four months. Retreatment cases received HRZE and streptomycin (S) for two months, followed by HRZE for one month and HRE for five months [2].

Statistical analysis

For statistical analyses, SPSS software version 15.0 was used. Descriptive statistics were presented as mean values with a standard deviation for numeric variables. In analytical statistics, a Chi-square test was used for categorical comparisons of the treatment outcome parameter, which was the primary endpoint of the study between subgroups, while Fisher's exact test was used for the appropriate parameters. For all statistical tests, the significance level (type I error, p) was considered as 0.05 (5%). A logistic regression analysis was used to calculate crude and adjusted odds ratio (OR) of successful treatment outcome at a 95% confidence interval (CI).

Ethical consideration

Written approval was obtained from the Ministry of Health to use data from the files of the tuberculosis patients. The study was approved by the institutional review board of Kocaeli University in accordance with the Helsinki recommendations (approval 2014/37).

Results

Sociodemographic and clinical characteristics

Of 738 bacteriologically confirmed PTB patients, most were male (65%) and younger than 50 years of age (71.2%). Most patients were employed (93.8%), covered by health insurance (86.7%), living in cities (91.1%), and in families of two to five people (73.6%). Sociodemographic characteristics are summarized in Table 1.

Most patients had newly diagnosed PTB (90%). Smear results on microscopy were positive for acid-fast bacilli in 88% of patients, whereas culture positivity was recorded in 96.7% of patients. Approximately one-third of patients had a comorbid disease, most commonly chronic lung disease. Drug resistance was detected in only 18% of patients, mainly to isoniazid. Radiography showed cavity in 34.8% of patients. Clinical characteristics are summarized in Table 2.

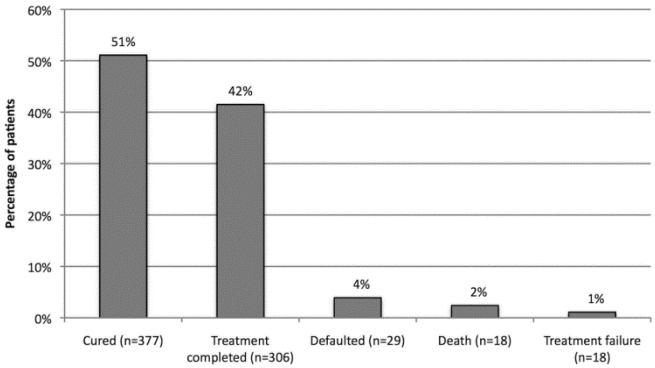
Treatment outcome

A total of 683 (92.6%) patients had a successful treatment outcome (cured or treatment completed), whereas 55 (7.4%) had an unsuccessful treatment outcome. Of those with a poor outcome, 29 (3.9%) had treatment default, 18 (2.4%) died, and 8 (1.1%) had treatment failure (Figure 1).

Factors associated with successful treatment outcome

On univariate analysis, it was revealed that younger patients, those without previous tuberculosis treatment, comorbidity, and drug resistance, and those with higher education had significantly higher prevalence of successful treatment outcome ($p < 0.05$ for all, Table 3). On multivariate analysis, the successful treatment outcome was 2.32-fold lower (95% CI, 0.59–9.15) in patients older than 65 years of age. The successful outcomes were 2.52-fold lower in the presence of previous treatment history (95% CI, 0.54–11.8). The presence of any comorbidity was associated with a 1.19-fold lower odds ratio (95% CI, 0.35–4.07). Successful outcomes were 1.08-fold lower (95% CI, 0.99–1.2) in the presence of any drug resistance, and the odds ratio was 1.6-fold lower in the presence of HR resistance (95% CI, 1.1–2.2). There was a significant association between having over five years of education and positive treatment outcomes ($p < 0.001$; OR, 0.26; CI 95%, 0.07–0.89) (Table 3).

Figure 1. Outcome of treatment in 738 patients with bacteriologically confirmed pulmonary tuberculosis.



Discussion

In the present study, the treatment success rate was 92.6% in bacteriologically confirmed PTB patients in Turkey. According to WHO data, in Turkey, the success rate was 90% in patients with a new culture or smear and 68% in retreatment cases in 2011 [5]. Based on 2011 data, the success rate was reported to be 72% for all new cases and 65% for new smear-positive patients in the European region (including Turkey), which shows that there is room for improvement [1].

The present study found that young age, drug resistance, previous treatment history, high education level, and absence of comorbidity were positively associated with successful treatment outcomes.

In two Turkish studies on the success of PTB treatment by Babalık *et al*., advanced age, male gender, being born abroad, history of treatment failure, previous history of tuberculosis treatment, and presence of antibiotic resistance and bilateral radiological lesion were associated with unsuccessful outcome. Another study showed that previous history of treatment, advanced age, and resistance to rifampicin were associated with treatment failure [6-8].

In the present study, the odds ratio for unsuccessful outcome was 2.5-fold higher in patients 55 years of age and older, and 5-fold higher in patients 65 years of age and older. In Turkey, Babalik *et al*. found that the treatment success rate was lower in patients 65 years of age and older, while Talay *et al*. showed that it was lower in patients 46 years of age and older [6,8]. Several studies have demonstrated an association between advance age and unsuccessful treatment outcomes. It is assumed to be related to increased comorbidity, overall physiological deterioration, and difficulty in accessing several healthcare opportunities along with increasing age [6,9-11].

Table 1. Sociodemographic characteristics of patients with pulmonary tuberculosis (n = 738)

		n (%)
Gender	Female	258 (35)
	Male	480 (65)
Age (years)	< 35	360 (48.8)
	35–50	165 (22.4)
	51–65	147 (19.9)
	> 65	66 (8.9)
Education	> 5 years	251 (44.1)
	≤ 5 years	318 (55.9)
Occupation	Unemployed	40 (6.2)
	Employed	602 (93.8)
	White collar	110 (17.1)
	Others	532 (82.9)
Health insurance	No	98 (13.3)
	Yes	640 (86.7)
Type of health insurance	Low-income insurance	545 (85.2)
	Other insurance	95 (14.8)
Family size	1	33 (49)
	2–5	496 (73.6)
	6+	145 (21.5)
Living area	Rural	65 (8.9)
	Central	666 (91.1)

The total number cases was less than 738 due to missing data for some parameters.

Table 2. Clinical characteristics of patients with pulmonary tuberculosis (n=738)

		n (%)
Smear acid-fast bacilli	Negative	80 (12)
	Positive	589 (88)
Culture	Negative	21 (3.3)
	Positive	609 (96.7)
Retreatment	No	661 (90.0)
	Yes	77 (10.0)
Comorbidity	No	522 (70.7)
	Yes	216 (29.3)
Comorbid diseases	Malignancy	14 (1.9)
	Chronic obstructive pulmonary disease	91 (12.4)
	Hypertension	16 (2.2)
	Diabetes mellitus	64 (8.7)
Drug resistance	No	383 (82)
	Yes	84 (18)
Type of drug resistance	Isoniazid	60 (12.8)
	Rifampicin	24 (5.1)
	Isoniazid + rifampicin	20 (4.9)
Cavity on radiography	No	481 (65.2)
	Yes	257 (34.8)

The total number cases was less than 738 due to missing data for some parameters.

Table 3. Clinical and sociodemographic factors and treatment outcomes of patients with bacteriologically confirmed pulmonary tuberculosis

		Successful treatment outcome n (%)	P value for univariate analysis[a]	Crude odds ratio (95% CI)	Adjusted odds ratio (95% CI)
Gender	Female	241 (93.4)	0.513	-1.0–	
	Male	442 (92.1)		1.0 (0.97–1.06)	
Age (years)	< 35	340 (94.4)	< 0.001	-1.0–	-1.0–
	35–50	154 (93.3)		1.5 (0.7–3.3)	0.34 (0.08–1.36)
	51–65	131 (89.1)		2.7 (1.31–5.6)	1.22 (0.38–3.90)
	> 65	54 (81.8)		4.9 (2.2–11)	2.32 (0.59–9.15)
Smear acid-fast bacilli	Negative	78 (97.5)	0.071	-1.0–	
	Positive	541 (91.9)		1.06 (1.0–1.1)	
Culture	Negative	19 (90.5)	0.67	1.0–	
	Positive	563 (92.4)		0.98 (0.85–1.12)	
Retreatment	No	618 (93.5)	0.004	-1.0–	-1.0–
	Yes	65 (84.4)		0.42 (0.23–0.75)	2.52 (0.54–11.8)
Comorbidity	No	497 (95.2)	< 0.001	-1.0–	-1.0–
	Yes	186 (86.1)		1.1 (1.0–1.2)	1.19 (0.35–4.07)
Comorbid disease	Malignancy	11 (78.6)		1.2 (0.9–1.6)	
	COPD	77 (84.6)	0.079	1.1 (1.01–1.2)	1.72 (0.32–9.09)
	Hypertension	13 (81.3)	0.002	1.1 (0.9–1.4)	
	Diabetes mellitus	57 (89.1)	0.110	1.0 (0.95–1.1)	
Drug resistance	No	358 (93.5)	0.024	-1.0–	NA
	Yes	73 (86.9)		1.08 (0.99–1.2)	NA
Type of drug resistance	Isoniazid	49 (81.7)	0.002	1.2 (1.0–1.3)	NA
	Rifampicin	16 (66.7)	< 0.001	1.4 (1.1–1.9)	NA
	Isoniazid + rifampicin	12 (60.0)	< 0.001	1.6 (1.1–2.2)	NA
Cavity on radiography	No	445 (92.5)	0.964	-1.0–	
	Yes	238 (92.6)		0.999 (0.96–1.04)	
Education	> 5 years	244 (97.2)	< 0.001	-1.0–	-1.0–
	≤ 5 years	280 (88.1)		0.91 (0.87–0.95)	0.26 (0.07–0.89)
Occupation	Unemployed	37 (92.5)	0.79	0.99 (0.9–1.1)	
	Employed	561 (93.2)		-1.0–	
Health insurance	No	91 (92.9)	0.900	-1.0–	
	Yes	592 (92.5)		1.0 (0.95–1.07)	
Type of health insurance	Low income insurance	507 (93.0)		1.040 (0.97–1.11)	
	Other insurance	85 (89.5)		-1.0–	
Family size	1	31 (93.9)	0.35	-1.0–	
	2–5	462 (93.1)		0.6 (0.1–2.6)	
	6+	130 (89.7)		0.6 (0.3–1.2)	
Living area	Rural	58 (89.2)	0.320	0.96 (0.88–1.05)	
	Central	618 (92.8)		-1.0–	

[a]Chi-square test; CI: confidence interval; COPD: chronic obstructive pulmonary disease; NA: not applicable: The total number cases was less than 738 due to missing data for some parameters.

The present study found that the presence of any additional disease and chronic lung disease was associated with adverse outcomes. A literature review of comorbid conditions showed that having any comorbid condition was associated with unsuccessful treatment outcomes, mainly death. Vasankari *et al*. found that the presence of immunosuppresion and malignity was associated with death, while the presence of any comorbid disease [7], diabetes mellitus and malignity [9], and diabetes mellitus [12-14] were associated with unsuccessful outcomes.

In the present study, the treatment success rate was lower in retreatment cases. Similarly, several studies found that previous treatment history was associated with unsuccessful treatment outcomes [8,15-17]. Some studies showed that previous defaulting was a risk factor for re-defaulting [12]. Furthermore, it may be associated with the increased frequency of drug resistance caused by previous suboptimal therapy. According to WHO data, the estimated incidence of multidrug-resistant TB (MDR-TB) in Turkey was 3.2% in new cases and 22% in retreatment cases in 2012 [5].

The presence of any drug resistance, particularly MDR, was associated with poor outcome. Babalık *et al*. found that treatment failure and resistance (particularly MDR) to any drug were associated with unsuccessful outcomes. Initial resistance to H in a study in Norway and any H or any R resistance in a Turkish study were found associated with treatment failure. Espinal *et al*. showed a correlation between treatment failure and only H resistance, any H resistance, and MDR [6,8,10,18].

In Turkey, the low-income insurance program provided to individuals with a low income level who do not have any other health insurance is considered as an index of low income level. No significant difference was found between the presence of low-income insurance and treatment success. There are some publications that reported an association between low income level and unsuccessful outcomes. Having a low income level was associated with treatment default in a study conducted in Kenya, and with poor treatment outcome in a Georgian study by Djibuti *et al*. [11,19]. The absence of any difference by income level can be attributed to insurance coverage of all individuals with a low income level, easy accessibility to healthcare professionals, and free-of-charge service for diagnostic and treatment services in dispensaries in Turkey.

The association between having an education level of five years or more and successful outcome was significant. Studies in Mexico, Brazil, and Georgia found a correlation between higher education level and treatment success [11,12,20]. In addition, Muture *et al*. evaluated having information about tuberculosis and showed that having enough information about the disease reduced the treatment default [19].

No association was found between gender and treatment success in our study. Several studies showed a lower rate of TB treatment in male patients, which may be attributed to social and environmental factors [17,21-23].

Some studies have found an association between demographic and clinical characteristics of patients (age, male gender, drug resistance, comorbidity, HIV co-infection, past history of TB, presence of activity on radiography) and negative treatment outcomes [9,10,13,24-26]. Additionally, various social and economic characteristics (lower education level, low income level, insufficient information about TB, living in rural areas, unemployment, alcoholism, and family size) have been found to be associated with negative treatment results [11,12,15,19,27-30]. In the present study, no association was observed with factors indicative of socioeconomic conditions such as occupational group, low-income health insurance program, living in rural areas, or living alone or with family; however, lower education level was associated with treatment failure. These findings may be attributed to the successful implementation of the DOT strategy for each socioeconomic group in our province.

The most important limitation of our study was that it was conducted retrospectively, based on available patient files. The present study does not include treatment outcomes of patients with tuberculosis and extrapulmonary tuberculosis who were not bacteriologically confirmed and who were younger than 15 years of age.

Conclusions

Young age, drug resistance, previous treatment history, high education level, and absence of comorbidities were predictors of successful outcome. It is believed that providing additional social and medical support for this group of patients, performing resistance tests for each retreatment case, and closely monitoring microbiological activity may contribute well to treatment success.

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References

1. World Health Organization (2013) Global Tuberculosis Report 2013. Available: http://www.who.int/tb/publications/global_report/en/. Accessed 9 July 2014.
2. Bozkurt H, Turkkanı MH, Musaonbaşıoğlu S (2011) Guideline for tuberculosis diagnosis and treatment. Ankara: Ministry of Health of Turkey Republic.
3. Bozkurt H, Turkkanı MH, Musaonbaşıoğlu S, Yıldırım A, Baykal F (2011) Fight against tuberculosis 2011 report of Turkey. Ankara: Ministry of Health of Turkey Republic.
4. Buzgan T, Torunoglu MA, Musaonbaşıoğlu S, Yıldırım A, Mutlu SM, Baykal F (2013) Fight against tuberculosis 2012 report of Turkey. Ankara: Ministry of Health of Turkey Republic.
5. World Health Organization (2014) Tuberculosis Country Profile. Available: http://www.who.int/tb/data. Accessed 9 July 2014.
6. Babalik A, Kilicaslan Z, Caner SS, Gungor G, Ortakoylu MG, Gencer S, McCurdy SA (2013) A registry-based cohort study of pulmonary tuberculosis treatment outcomes in Istanbul, Turkey. Jpn J Infect Dis 66: 115-120.
7. Babalik A, Kilicaslan Z, Kiziltas S, Gencer S, Ongen G (2013) A retrospective case-control study, factors affecting treatment outcomes for pulmonary tuberculosis in Istanbul, Turkey. Balkan Med J 30: 204-210.
8. Talay F, Kumbetli S, Altin S (2008) Factors associated with treatment success for tuberculosis patients: a single center's experience in Turkey. Jpn J Infect Dis 61: 25-30.
9. Vasankari T, Holmström P, Ollgren J, Liippo K, Kokki M, Ruutu P (2007) Risk factors for poor tuberculosis treatment outcome in Finland: a cohort study. BMC Public Health 7: 291.
10. Farah MG, Tverdal A, Steen TW, Heldal E, Brantsaeter AB, Bjune G (2005) Treatment outcome of new culture positive pulmonary tuberculosis in Norway. BMC Public Health 5: 14.
11. Djibuti M, Mirvelashvili E, Makharashvili N, Magee MJ (2014). Household income and poor treatment outcome among patients with tuberculosis in Georgia: a cohort study. BMC Public Health 14: 88.
12. Garrido Mda S, Penna ML, Perez-Porcuna TM, de Souza AB, Marreiro Lda S, Albuquerque BC, Martínez-Espinosa FE, Bührer-Sékula S (2012) Factors associated with tuberculosis treatment default in an endemic area of the Brazilian Amazon: a case control-study. PLoS One 7: e39134.
13. Tang S, Tan S, Yao L, Li F, Li L, Guo X, Liu Y, Hao X, Li Y, Ding X, Zhang Z, Tong L, Huang J (2013) Risk factors for poor treatment outcomes in patients with MDR-TB and XDR-TB in China: retrospective multi-center investigation. PLoS One 8: e82943.
14. Mi F, Tan S, Liang L, Harries AD, Hinderaker SG, Lin Y, Yue W, Chen X, Liang B, Gong F, Du J (2013) Diabetes mellitus and tuberculosis: pattern of tuberculosis, two-month smear conversion and treatment outcomes in Guangzhou, China. Trop Med Int Health 18: 1379-1385.
15. Berhe G, Enquselassie F, Aseffa A (2012) Treatment outcomes of smear-positive pulmonary tuberculosis patients in Tigray Region, Northern Ethiopia. BMC Public Health 12: 537.
16. de Albuquerque Mde F, Ximenes RA, Lucena-Silva N, de Souza WV, Dantas AT, Dantas OM, Rodrigues LC (2007) Factors associated with treatment failure, dropout, and death in a cohort of tuberculosis patients in Recife, Pernambuco State, Brazil. Cad Saude Publica 23: 1573-1582.
17. Muñoz-Sellart M, Cuevas LE, Tumato M, Merid Y, Yassin MA (2010) Factors associated with poor tuberculosis treatment outcome in the Southern Region of Ethiopia. Int J Tuberc Lung Dis 14: 973-979.
18. Espinal MA, Kim SJ, Suarez PG, Kam KM, Khomenko AG, Migliori GB, Baéz J, Kochi A, Dye C, Raviglione MC (2000) Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries. JAMA 283: 2537-2545.
19. Muture BN, Keraka MN, Kimuu PK, Kabiru EW, Ombeka VO, Oguya F (2011) Factors associated with default from treatment among tuberculosis patients in Nairobi province, Kenya: A case control study. BMC Public Health 11: 696.
20. García-García Mde L, Ponce-De-León A, García-Sancho MC, Ferreyra-Reyes L, Palacios-Martínez M, Fuentes J, Kato-Maeda M, Bobadilla M, Small P, Sifuentes-Osornio J (2002) Tuberculosis related deaths within a well-functioning DOTS control program. Emerg Infect Dis 8: 1327-1333.
21. Falzon D, Le Strat Y, Belghiti F, Infuso A (2005) Exploring the determinants of treatment success for tuberculosis cases in Europe. Int J Tuberc Lung Dis 9: 1224-1229.
22. Karim F, Ahmed F, Begum I, Johansson E, Diwan VK (2008) Female-male differences at various clinical steps of tuberculosis management in rural Bangladesh. Int J Tuberc Lung Dis 12: 1336-1339.
23. Somma D, Thomas BE, Karim F, Kemp J, Arias N, Auer C, Gosoniu GD, Abouihia A, Weiss MG (2008) Gender and sociocultural determinants of TB-related stigma in Bangladesh, India, Malawi and Colombia. Int J Tuberc Lung Dis 12: 856-866.
24. Lin CH, Lin CJ, Kuo YW, Wang JY, Hsu CL, Chen JM, Cheng WC, Lee LN (2014) Tuberculosis mortality: patient characteristics and causes. BMC Infect Dis 14: 5.
25. Antoine D, French CE, Jones J, Watson JM (2007) Tuberculosis treatment outcome monitoring in England, Wales and Northern Ireland for cases reported in 2001. J Epidemiol Community Health 61: 302-307.
26. Kliiman K, Altraja A (2010) Predictors and mortality associated with treatment default in pulmonary tuberculosis. Int J Tuberc Lung Dis 14: 454-463.
27. Pefura Yone EW, Kengne AP, Kuaban C (2011) Incidence, time and determinants of tuberculosis treatment default in Yaounde, Cameroon: a retrospective hospital register-based cohort study. BMJ Open 1: e000289.
28. Wobeser W, Yuan L, Naus M (1999) Outcome of pulmonary tuberculosis treatment in the tertiary care setting - Toronto 1992/93. Tuberculosis Treatment Completion Study Group. CMAJ 160: 789-794.
29. Finlay A, Lancaster J, Holtz TH, Weyer K, Miranda A, van der Walt M (2012) Patient- and provider-level risk factors associated with default from tuberculosis treatment, South Africa, 2002: a case-control study. BMC Public Health 12: 56.
30. Bumburidi E, Ajeilat S, Dadu A, Aitmagambetova I, Ershova J, Fagan R, Favorov MO (2006) Progress toward tuberculosis control and determinants of treatment outcomes--Kazakhstan, 2000-2002. MMWR Morb Mortal Wkly Rep 55 Suppl 1: 11-15.

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