Impact of Diabetes Mellitus on Treatment Outcomes of Tuberculosis Patients in Tertiary Care Setup

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Abstract: *Background:* Concurrent diabetes mellitus (DM) with tuberculosis (TB) has an increased risk of treatment failure. This study was aimed to evaluate treatment outcomes in patients with TB with and without DM. *Methods:* A retrospective cohort study was conducted at respiratory clinic of Hospital Pulau Pinang, Malaysia. All TB-registered patients from January 2006 to December 2007 were included in the study. A validated data collection form was used for collecting data. World Health Organization's criterion was used for categorizing treatment outcomes. Data were analyzed by using SPSS 16. *Results:* Of 1267 patients, 338 patients (26.7%) had concurrent TB-DM. In multivariate analysis, TB-DM was more likely to be present in Chinese (odds ratio [OR] = 1.401, $P = 0.011$), patients having age of 46 to 60 years (OR = 3.168, $P < 0.001$) and >60 years (OR = 2.524, $P < 0.001$) and patients with pulmonary TB (OR = 2.079, $P < 0.001$). Nine hundred and eighty-five (78.8%) patients were successfully treated. No statistically significant difference was observed between 2 groups: patients with TB-DM and patients with only TB. Successful treatment outcomes were observed in patients having age of 46 to 60 (OR = 1.567, $P = 0.001$), whereas male gender (OR = 0.721, $P = 0.049$) and patients with relapse TB (OR = 0.494, $P = 0.002$) were less likely to have successful treatment outcome. *Conclusions:* High prevalence of TB-DM in the study signifies the fact that patients with DM are at high risk of developing TB. Treatment outcomes in both groups were comparable. The gender-based and age-based disparity in TB treatment outcomes in this study indicates the importance of gender-specific and age-specific strategies of TB management.

Key Indexing Terms: Diabetes mellitus; Treatment outcomes; Tuberculosis. **[Am J Med Sci 2013;345(4):321–325.]**

Tuberculosis (TB), an infectious disease caused by *Mycobecterium tuberculosis*, is a critical health problem globally. It is the second leading cause of death from an infectious disease worldwide. Despite the availability of highly efficacious pharmacotherapy, TB still remains as a major public health problem globally with an estimated 8.5 to 9.2 million cases and 1.2 to 1.5 million deaths in 2010.[1] Epidemiological studies have reported a strong association between TB and diabetes mellitus (DM).[2,3] It is found that people suffering from DM are approximately 3 times more prone to developing TB as compared with people without DM.[2] Various case-control studies have reported poor TB treatment outcomes in patients suffering with TB-DM as compared with only TB.[4,5] The prevalence of DM increasing worldwide is projected to reach an approximate total of 300 million by 2025, and more than 75% of the diabetic population will be harbored by developing and newly developed countries.[6] Similar to what is reported worldwide, increase in the prevalence of DM (8.3% in 1996 to 11.6% in 2006) is observed in Malaysia.[7] Although TB prevalence in Malaysia has decreased enormously as compared with the early 1990s, but still Malaysia is ranked 15th in TB burden in Western Pacific Region by the World Health Organization (WHO) in 2010 with a prevalence rate of 107/100,000 and estimated mortality rate of 8.5/100,000 (excluding HIV) as compared with the prevalence rate of 227/100,000 and mortality rate of 24/100,000 (excluding HIV) in 1990.

Despite the increase in the prevalence of DM in Malaysia, association between the prevalence of TB and DM and impact of DM on TB treatment outcomes, the information about impact of DM in TB prevalence and its outcomes is scarce. This study was conducted with the aim to determine factors associated with the presence of TB-DM and TB treatment outcomes.

METHODS

A retrospective cohort study was conducted at respiratory clinic of Hospital Pulau Pinang, Malaysia, the main referral hospital for the management of patients with TB and suspects in Pulau Pinang, North Malaysia. All patients with TB who were presented to the clinic from January 2006 to December 2007 were included in the study. Patients with TB with human immunodeficiency virus (HIV), hepatitis B, C or both, end-stage renal failure, immunosuppression due to organ transplantation, cancer and patients with incomplete medical record were excluded from the study. A purpose-developed valid data collection form was used for collecting demographic and clinical data. Demographic data included patients' gender, age, weight, ethnicity, residential area, marital status, smoking and alcohol consumption status. Age and weight first recorded as continuous data were then classified into categories. Clinical data collected included clinical presentation, serum biochemistry results, nature of TB case [new, retreatment (failure, default and relapse)], site of TB infection (pulmonary, extrapulmonary and pulmonary + extrapulmonary), with confirmed DM, TB and DM medications, results of sputum culture and treatment outcomes. Disease classification, treatment protocol and treatment outcomes were defined as per WHO guidelines (Reference). Sputum smear examinations were done at the end of 2, 4 and 6 months of treatment in new cases and at the end of 2, 3, 5 and 8 months in retreatment cases. Sputum examination was repeated again after 1 month if positive at 2 months of treatment.

Treatment outcomes initially recorded as cured, treatment completed, defaulted, transferred out, expired and treatment continued were then classified into 2 categories successful and unsuccessful treatment. Cured and treatment-completed patients

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were placed in treatment successful category whereas the rest were placed in the category of unsuccessful treatment.

Statistical Analysis

Data were analyzed using SPSS 16. Percentages and frequencies were used for categorical variables, and means and standard deviations were calculated for continuous variables. Univariate analysis was used to observe significance between categorical variables, whereas multivariate binary regression analysis is used when required. The results of multivariate binary regression analysis were presented as beta, standard error, *P*-value, adjusted odd ratio and 95% confidence interval. The fit of the model was assessed by Hosmer Lemeshow and overall classification percentage. Significance of the statistical tests was taken at a *P*-value of <0.05. This study was approved by the Clinical Research Centre hospital Pulau Pinang and Ministry of Health, Malaysia research ethics committee.

RESULTS

Factors Associated With the Prevalence of TB DM

A total of 1267 patients with TB were included in the final analysis. Three hundred and thirty-eight patients (26.7%) had coexisting TB-DM. Patient's demographic and clinical characteristics are given in Table 1. Statistically significant difference (*P*-value < 0.001) was observed in patients' mean age with only TB (41.44 ± 16.5) and with TB-DM [(50.69 ± 13.0) and (median age 50.00), age limits were 12–91 years old]. TB-DM was more prevalent in Chinese (*P*-value = 0.006), married (*P*-value = 0.004) and patients suffering from pulmonary TB (*P*-value < 0.001) (Table 1).

The independent predictors that had significant association with the presence of TB-DM were included into a multivariate analysis. In multivariate analysis, TB-DM was more likely to be present in Chinese (odds ratio [OR] = 1.401, *P*-value = 0.011), patients having age 46 to 60 years (OR = 3.168, *P*-value < 0.001), and >60 years (OR = 2.524, *P*-value < 0.001) and patients with pulmonary TB (OR = 2.079, *P*-value < 0.001). This model fit was based on a nonsignificant Hosmer and Lamshow test (*P*-value = 0.403) and overall percentage of 73.3% from the classification table (Table 2).

TB Treatment Outcomes

Nine hundred and eighty-five patients (78.8%) were successfully treated. Among 985 successfully treated patients, 808 patients were cured, whereas 177 completed their treatment. Among 281 unsuccessfully treated patients (22.2%), 61 patients died, 42 defaulted, 38 transferred out and 140 were on treatment continued. In terms of treatment outcomes, no statistically significant difference (*P*-value = 0.514) was observed between 2 groups: patients with TB-DM and patients with only TB. In TB-DM group, 76.3% of patients were treated successfully, whereas in TB-only group, 78.3% of patients were treated successfully (Tables 3 and 4).

Factors Associated With Treatment Outcomes

On univariate analysis, it was found that treatment outcome had significant association with patients' age, gender, smoking status, TB history (new or relapse) and site of infection (Table 5).

The independent predictors that had significant association with treatment outcome in univariate analysis were included into multivariate analysis. Successful treatment outcome was observed in patients having age of 46 to 60 years (OR = 1.567, *P*-value = 0.001), whereas male gender (OR = 0.721, *P*-value = 0.049) and patients with relapse TB (OR = 0.494, *P*-value = 0.002) were less likely to have successful treatment outcome (Table 6). This model fit was based on a nonsignificant Hosmer and Lamshow test (*P* = 0.985) and overall percentage of 76.5% from the classification table.

TABLE 1. Demographic profile and other characteristics of patients studied

Variables	TB-DM	Only TB	χ^2	df	*P*
Gender			0.033	1	0.903[b]
Male	243 (26.5)	673 (73.5)			
Female	95 (27.1)	256 (72.9)			
Age (yr)	50.69 ± 13.0	41.44 ± 16.5	16.5	1	0.000[a]
≤30	12 (4.2)	251 (95.8)			
31–45	106 (26.0)	301 (74.0)			
45–60	141 (39.7)	214 (60.3)			
>60	79 (35.7)	142 (64.3)			
Ethnicity			12.4	3	0.006[b]
Chinese	176 (31.5)	382 (68.5)			
Malay	101 (22.2)	353 (77.8)			
Indian	42 (24.1)	132 (75.9)			
Others	19 (23.5)	62 (76.5)			
Area			0.051	1	0.911[b]
Rural	307 (26.8)	840 (73.2)			
Urban	31 (25.8)	89 (74.2)			
Smoking			0.571	1	0.482[b]
Yes	135 (27.9)	203 (25.9)			
No	349 (72.1)	580 (74.1)			
Alcohol consumption			1.508	1	0.259[b]
Yes	40 (31.2)	298 (26.2)			
No	88 (68.8)	841 (73.8)			
Marital status			8.257	1	0.121[b]
Married	190 (18.6)	827 (81.4)			
Unmarried	48 (19.2)	202 (80.8)			
TB location			17.616	2	0.000[b]
PTB	303 (29.0)	741 (71.0)			
Extra PTB	30 (17.1)	145 (82.9)			
PTB + extra PTB	5 (10.4)	43 (89.6)			

[a] Student's *t* test.
[b] χ^2.
PTB, pulmonary TB.

TABLE 2. Multivariate analysis of predictors of prevalence of TB-DM

Variable	B	SE	*P*	OR	95% CI
Chinese[a]	0.337	0.133	0.011	1.401	1.079–1.818
Age (yr)[b]					
46–60	1.153	0.150	<0.001	3.168	2.359–4.253
>60	0.926	0.175	<0.001	2.524	1.791–3.558
Pulmonary TB[c]	0.732	0.202	<0.001	2.079	1.398–3.558

Only significant results are given in the table.
[a] Reference category: Malay.
[b] Reference category: age #30 years.
[c] Reference category: extrapulmonary TB.
CI, confidence interval.

TABLE 3. Overall treatment outcome

Treatment outcome	n (%)
Successful	985 (77.8)
Cured	808 (63.82)
Treatment completed	177 (13.98)
Unsuccessful	281 (22.2)
Death	61 (4.82)
Defaulted	42 (3.31)
Transferred out	38 (3.0)
Treatment continued	140 (11.05)

DISCUSSION

DM is rising worldwide especially in developing countries. In this study, the prevalence to TB among patients with DM is quite high due to exclusion criteria. This study shows that 26.7% of patients with TB had coexisting DM; a rate twice of the prevalence of DM (11.8%) in Malaysian general population.[7] In our study, DM antedated TB by a mean of 3.5 years. Because DM acts as a risk factor for the development of TB by causing hyperglycemia, cellular insulinopenia, and affecting macrophage and lymphatic system of the host,[8] high prevalence of coexisting TB-DM in this study is not astonishing. This finding is comparable to a study conducted in Mexico, which has reported DM prevalence of 5.3% in general population and 35% in patients with TB.[9] It is also in line with various other studies conducted elsewhere and Malaysia and strengthens the previously reported increased incidence of TB-DM.[10–12]

This study revealed that patients with TB-DM were significantly older than TB-only patients. In multivariate analysis, it is observed that older age (≥46 years) had statistically significant positive association with TB-DM. Similar association between older age and presence of TB-DM has been observed in studies conducted in Saudi Arabia and Malaysia.[10,13] The reason for this association seems to be increased risk of developing DM in older age.[14,15] In this study, Chinese ethnicity had a statistically significant positive association with TB-DM. The reason for this finding is not clear and could be a random occurring but is in line with one of the studies conducted in Malaysia,[12] and at the same time is in disagreement with another in which no association has been observed between Chinese ethnicity and TB-DM.[13] A large study in future is needed to confirm this finding. Multivariate analysis in this study revealed that TB-DM is 2 times more prevalent in pulmonary TB as compared with extrapulmonary TB. This finding is supported by various other studies conducted in Malaysia and elsewhere that have reported an association between DM and pulmonary TB.[12,13,16,17] Positive association between DM and pulmonary TB might be due to the increased susceptibility of diabetic patients to certain respiratory tract infections including TB.[18] However, a study conducted in Turkey did not find any association between DM and pulmonary TB.[19]

In this study, more than three fourth of the patients (77.8%) were treated successfully. Treatment success rate in this study is well behind the WHO's target of 85%. Almost similar treatment success rates (78.8% and 78%) were reported in 2006 to 2008.[20,21] Cure rate (63.82%) in our study is lower than WHO targets for TB control. Low cure rates can increase the rate of the transmission of the disease and should be taken seriously.

No statistically significant difference was observed in treatment outcomes of TB-DM and TB-only patients. In this study, favorable and unfavorable outcomes were comparable in both groups of patients. Results reported by previous studies also vary in this regard. In a descriptive case-control study, 41% treatment failure was observed in patients with TB-DM as compared with 13% in TB-only patients.[4] In a retrospective study conducted in Taiwan, a high percentage (12.2%) of TB attributed death was seen in patients with TB-DM as compared with 4.2% in TB-only patients.[22] Similarly, in a study conducted in Malaysia, a higher mortality rate of 7.5% was observed in patients with TB-DM as compared with 1% in TB-only patients.[12] Majority of the studies that have reported DM as a risk factor for treatment failure have failed to report causes of death, and whether if death is caused by severity of TB or existence of comorbidities attributable to DM and compounded by older age make the studies unclear.[8] This potential limitation might have caused drawing an exaggerative false-positive conclusion of DM as a risk factor for treatment failure. On the other hand, similar to our finding, various studies have reported no association between DM and TB treatment outcomes. In a study conducted in Saudi Arabia, no statistically significant difference was observed in treatment outcomes of TB only and patients with TB-DM.[10] Similarly, no statistically significant difference was observed in treatment outcomes of TB-DM and TB-only patients in studies conducted in Taipei,[23] Finland[24] and Thailand.[25]

In multivariate analysis, male gender had statistically significant negative association with successful treatment outcome. This finding is in agreement with various other studies conducted elsewhere. In a study conducted in India, men had 2 times greater risk of treatment failure than women.[26] Male gender was also found to be associated with poor treatment outcomes in a studies conducted in Nigeria,[27] Taiwan[28] and Saudi Arabia.[29] One of the reasons for poor treatment outcomes in men might be their nonadherence with therapy as described by other studies,[26,28,29] whereas the other possibility might be different hormonal effects. Differences in sexual hormones may lead to TB treatment outcomes inequalities between genders.[28] For example, mice studies have demonstrated that ovariectomized mice are more susceptible to *Mycobacterium avium* infection and the estradiol may reverse the greater vulnerability.[30] However, some studies have reported similar treatment outcomes in both men and women.[31,32]

In this study, older age (46–60 year) has statistically negative association with successful treatment outcomes. Similar to our finding, a study conducted in Turkey has also stated the age in excess of 46 years as a risk factor for poor treatment outcomes.[33] General physiological deterioration with age, compromised immunity in elderly, less able to reach health facilities are the various reasons for poor TB treatment outcomes in older age.[34] This finding is supported by various studies conducted

TABLE 4. Treatment outcome in patient with and without DM

	Successfully treated			Unsuccessfully treated				Total	
Variable	Cured	Treatment completed	Total n (%)	Death	Defaulted	Transferred out	Treatment continued	n (%)	*P*
TB DM	214	44	258 (76.3)	19	12	11	42	84 (23.7)	0.514
Only TB	594	123	727 (78.3)	42	30	27	98	197 (21.7)	

TABLE 5. Univariate analysis of predictors of treatment outcome

Variables	Treatment outcome, n (%)		P	95% CI	OR
	Successful	Unsuccessful			
Gender			0.009	0.489–0.905	0.665
Male	693 (75.7)	222 (24.3)			
Female	292 (83.2)	59 (16.8)			
TB case			0.003	0.327–0.802	0.512
Retreatment	61 (67.0)	30 (33.0)			
New	924 (78.6)	251 (21.4)			
Smoking			0.029	0.572–0.970	0.745
Yes	359 (74.2)	125 (25.8)			
No	626 (80.1)	156 (19.9)			
Extrapulmonary TB			0.020	1.081–2.511	1.648
Yes	146 (83.4)	29 (16.6)			
No	839 (76.9)	252 (23.1)			
Age (yr)*					
31–45			0.010	0.534–0.919	0.701
Yes	297 (73.0)	110 (27.0)			
No	688 (80.1)	171 (19.9)			
46–60			0.002	1.210–2.256	1.652
Yes	302 (85.1)	53 (14.9)			
No	683 (75.0)	228 (25.0)			

Only significant results are given in the table.
SE, standard error; CI, confidence interval.

elsewhere.[25,34,35] However, it is interesting to note that in this study, the extreme advance age of >60 years was not associated with poor treatment outcomes. This finding needs further research to identify the reasons for better treatment outcomes in patients of age >60 as compared with those 46 to 60 years. One of the possible reasons for this finding might be that patients of age >60 usually do not work and live retired life where the chances of default are quite lower as compared with those patients who do work. Demand of work seems one of the major reasons of poor treatment outcomes in patients of age 46 to 60 years.

Retreatment TB was another factor associated with poor treatment outcomes in this study. It is a well-known fact that most of the times, retreatment outcomes are often poor.[36,37] This finding is a clear indication of the importance of properly managing and completing anti-TB therapy the first time around. Prior ineffective treatment has been widely recognized as is a strong predictor of drug-resistant TB in the majority studies conducted in various parts of the world.[38–40]

TABLE 6. Multivariate analysis of predictors of treatment outcome

Variable	B	SE	P	OR	95% CI
Male[a]	−0.327	0.166	0.049	0.721	0.521–0.999
Retreatment TB[b]	−0.704	0.232	0.002	0.494	0.314–0.779
Age (46–60 yr)[c]	0.449	0.176	0.001	1.567	1.110–2.214

Only significant results are given in the table. Hosmer Lamshow = 0.985, overall percentage = 76.5.
[a] Reference category: female.
[b] Reference category: newly diagnosed TB.
[c] Reference category: age 15–30 years.
SE, standard error; CI, confidence interval; SE, standard error.

CONCLUSIONS

High prevalence of TB-DM in this study signifies the fact that patients with DM are at high risk of developing pulmonary TB. Increase in the prevalence of DM in intermediate TB burden country like Malaysia makes it a worrisome issue and should have important implications on prioritization of health care. This study confirmed that association of DM has no effects on TB treatment outcomes. Treatment outcomes in both groups were comparable. Due to retrospective nature of the study, we were unable to evaluate the DM control status of the patients that whether it had any impact on treatment outcomes. The gender-based and age-based disparity in TB treatment outcomes in this study indicates the importance of gender-specific and age-specific strategies of TB management. Poor treatment outcomes in retreatment patients signify the importance of properly completing anti-TB therapy for the first time around and evaluating such patients for drug-resistant TB.

LIMITATION AND FUTURE DIRECTION

This study was hospital based, and the same trend might not be seen in general population. To confirm the prevalence, a large study of TB screening in diabetic patients is suggested.

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REFERENCES

1. **WHO.** Global tuberculosis control: WHO Report. World Health Organization; 2011. p. 246.

2. **Jeon CY, Murray MB.** Diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. PLoS Med 2008;5:e152.
3. **Stevenson CR, Critchley JA, Forouhi NG, et al.** Diabetes and tuberculosis: the impact of the diabetes epidemic on tuberculosis incidence. BMC Public Health 2007;7:234.
4. **Mboussa J, Monabeka H, Kombo M, et al.** [Course of pulmonary tuberculosis in diabetics]. Revue de pneumologie clinique 2003;59:39.
5. **Morsy AM, Zaher HH, Hassan MH, et al.** Predictors of treatment failure among tuberculosis patients under DOTS strategy in Egypt. East Mediterr Health J 2003;9:689–701.
6. **King H, Aubert RE, Herman WH.** Global burden of diabetes, 1995â €"2025: prevalence, numerical estimates, and projections. Diabetes care 1998;21:1414–31.
7. **Letchuman GR, Wan Nazaimoon WM, Wan Mohammad WB, et al.** Prevalence of diabetes in the Malaysian national health Morbidity Survey III 2006. Med J Malaysia 2010;65:173.
8. **Dooley KE, Chaisson RE.** Tuberculosis and diabetes mellitus: convergence of two epidemics. Lancet Infect Dis 2009;9:737–46.
9. **Ponce-de-Leon A, Garcia MLG, Sancho MCG, et al.** Tuberculosis and diabetes in southern Mexico. Diabetes Care 2004;27:1584–90.
10. **Singla R, Khan N, Al-Sharif N, et al.** Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients. Int J Tuberc Lung Dis 2006;10:74.
11. **Mugusi F, Swai AB, Alberti KG, et al.** Increased prevalence of diabetes mellitus in patients with pulmonary tuberculosis in Tanzania. Tubercle 1990;71:271–6.
12. **Syed Sulaiman SA, Daud MIA, Ali JM, et al.** Role of diabetes in the prognosis and therapeutic outcome of tuberculosis. Int J Endocrinol 2012;2012:645362.
13. **Nissapatorn V, Kuppusamy I, Jamaiah I, et al.** Tuberculosis diabetic patients: a clinical perspective. 2005.
14. **Harris MI, Katherine MF, Mark SE, et al.** Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in US population aged 20-74 yr. Diabetes 1987;36:523–34.
15. **Morley JE.** The elderly type 2 diabetic patient: special considerations. Diabet Med 1998;15:41–6.
16. **Sreeramareddy CT, Panduru KV, Verma SC, et al.** Comparison of pulmonary and extrapulmonary tuberculosis in Nepal—a hospital-based retrospective study. BMC Infect Dis 2008;8:8.
17. **Shetty N, Shemko M, Vaz M, et al.** An epidemiological evaluation of risk factors for tuberculosis in South India: a matched case control study. Int J Tuberc Lung Dis 2006;10:80–6.
18. **Joshi N, Caputo GM, Weitekamp MR, et al.** Infections in patients with diabetes mellitus. New England J Med 1999;341:1906–12.
19. **Musellim B, Erturan S, Sonmez E, et al.** Comparison of extra-pulmonary and pulmonary tuberculosis cases: factors influencing the site of reactivation. Int J Tuberc Lung Dis 2005;9:1220–3.
20. **Dujaili JA, Syed Azhar SS, Awaisu A, et al.** Outcomes of tuberculosis treatment: a retrospective cohort analysis of smoking versus non-smoking patients in Penang, Malaysia. J Public Health 2011;19:183–9.
21. **Patton GC, Coffey C, Sawyer SM, et al.** Global patterns of mortality in young people: a systematic analysis of population health data. Lancet 2009;374:881–92.
22. **Wang CS, Yang CJ, Chen HC, et al.** Impact of type 2 diabetes on manifestations and treatment outcome of pulmonary tuberculosis. Epidemiol Infect 2009;137:203–10.
23. **Chiang CY, Lee JJ, Yu MC, et al.** Tuberculosis outcomes in Taipei: factors associated with treatment interruption for 2 months and death. Int J Tuberc Lung Dis 2009;13:105–11.
24. **Vasankari T, Holmstrom P, Pllgren J, et al.** Risk factors for poor tuberculosis treatment outcome in Finland: a cohort study. BMC Public Health 2007;7:291.
25. **Anunnatsiri S, Chetchotisakd P, Wanke C.** Factors associated with treatment outcomes in pulmonary tuberculosis in northeastern Thailand. 2005.
26. **Balasubramanian R, Garg R, Santha T, et al.** Gender disparities in tuberculosis: report from a rural DOTS programme in south India. Int J Tuberc Lung Dis 2004;8:323–32.
27. **Fatiregun AA, Ojo AS, Bamgboye AE.** Treatment outcomes among pulmonary tuberculosis patients at treatment centers in Ibadan, Nigeria. Ann Afr Med 2009;8.
28. **Feng JY, Huang SF, Ting WY, et al.** Gender differences in treatment outcomes of tuberculosis patients in Taiwan: a prospective observational study. Clin Microbiol Infect 2012.
29. **Samman Y, Krayem A, Haidar M, et al.** Treatment outcome of tuberculosis among Saudi nationals: role of drug resistance and compliance. Clin Microbiol Infect 2003;9:289–294.
30. **Tsuyuguchi K, Suzuki K, Matsumoto H, et al.** Effect of oestrogen on Mycobacterium avium complex pulmonary infection in mice. Clin Exp Immunol 2001;123:428–34.
31. **Belo MTCT, Luiz RR, Christy H, et al.** Tuberculosis and gender in a priority city in the state of Rio de Janeiro, Brazil. Jornal Brasileiro de Pneumologia 2010;36:621–5.
32. **Kamel MI, Moustafa YA, Foda N, et al.** Gender differences in health care utilization and outcome of respiratory tuberculosis in Alexandria. East Mediterr Health J 2003;9:741–56.
33. **Talay F, Kumbetli S, Altin S.** Factors associated with treatment success for tuberculosis patients: a single center's experience in Turkey. Jpn J Infect Dis 2008;61:25.
34. **Berhe G, Enquselassie F, Aseffa A.** Treatment outcome of smear-positive pulmonary tuberculosis patients in Tigray Region, Northern Ethiopia. BMC Public Health 2012;12:537.
35. **Munoz-Sellart M, Cuevas LE, Tumoto M, et al.** Factors associated with poor tuberculosis treatment outcome in the Southern Region of Ethiopia. Int J Tuberc Lung Dis 2010;14:973–9.
36. **Ottmani SE, Zignol M, Bencheikh N, et al.** Results of cohort analysis by category of tuberculosis retreatment cases in Morocco from 1996 to 2003. Int J Tuberc Lung Dis 2006;10:1367–72.
37. **Mak A, Thomas A, del Granado M, et al.** Influence of multidrug resistance on tuberculosis treatment outcomes with standardized regimens. Am J Respir Crit Care Med 2008;178:306–12.
38. **Caminero JA.** Management of multidrug-resistant tuberculosis and patients in retreatment. Eur Respir J 2005;25:928–36.
39. **Shamaei M, Marjani M, Chisaz E, et al.** First-line anti-tuberculosis drug resistance patterns and trends at the national TB referral center in Iran—eight years of surveillance. Int J Infect Dis 2009;13:e236–40.
40. **Liang L, Wu Q, Gao L, et al.** Factors contributing to the high prevalence of multidrug-resistant tuberculosis: a study from China. Thorax 2012;doi:10.1136/thoraxjnl-2011-200018.