A nested case-control study on relapse predictors among tuberculosis patients treated in Yemen's NTCP

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Setting: The National Tuberculosis (TB) Control Programme in Yemen.

Objective: To identify risk factors associated with TB relapse.

Methods: In a prospective nested case-control study, relapse cases were recruited from a cohort of pulmonary TB patients registered between July 2007 and June 2008. Four controls per case were randomly selected from the list of non-relapse patients. Three forms were used for data collection, which included interviews with the participants and review of their medical cards and TB registers. Multivariate logistic regression analysis was performed to identify independent risk factors for relapse.

Results: A relapse rate of 5.7% was found. Multivariate logistic regression analysis showed that unemployment, smoking, presence of cavitations, weight gain, weight loss, non-adherence during the continuation phase and diabetes were significantly associated with relapse ($P < 0.05$).

Conclusion: Relapse rates can be reduced by ensuring that patients take their treatment regularly and are counselled effectively to stop smoking. Reinforcing the implementation of the DOTS strategy and strengthening the anti-smoking campaigns are important actions. Action to help unemployed patients, including free services and the creation of new job opportunities, should be adopted. Using rifampicin-based regimens in the treatment of cavitary TB and bi-directional screening in TB and diabetes patients are recommended.

Tuberculosis (TB) is a major public health problem in Yemen, ranking fourth in the list of priority public health issues. Based on Yemen's national statistics, it is estimated that TB is the fourth leading cause of death. According to National TB Control Programme (NTCP) guidelines,¹ the latest estimated incidence rate of new smear-positive TB was 25 per 100 000 population. From 1995 to 2009, numbers of new smear-positive TB cases ranged from 3681 to 3576, in a total population of about 24 million. In Yemen's NTCP, based on the DOTS strategy, patients are treated with a daily short-course treatment regimen consisting of an initial 2-month intensive phase of isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E), followed by a 6-month continuation phase of HE (4HRZE/6HE). According to the 2010 World Health Organization (WHO) report² and unpublished data from the statistics department of the NTCP, Yemen has achieved a treatment success rate of 85%. However, the relapse rate, which is also an important indicator of the success of any treatment regimen, has not been measured under programme conditions. Available data showed a

high relative relapse rate (RRR) of 6–11% between 1995 and 2009, exceeding the acceptable norm ($<5\%$).^{3–5} The present study was designed to measure the actual relapse rate and to identify associated risk factors.

METHODS

Study design

A prospective nested case-control study was conducted to identify risk factors for relapse among TB patients. At the end of the follow-up period (28 February 2010), all those who relapsed within 12 months after completion of treatment were identified from the tuberculosis registry. For each confirmed relapse case, four control subjects were randomly selected from among patients who had successfully completed the initial phase of treatment and had not relapsed. Sampling was performed using the Statistical Package for the Social Sciences sampling procedure (Base 7.4 for Windows, SPSS Inc, Chicago, IL, USA).

Study area and population

The study was conducted at health centres with TB units throughout the 10 governorates of Yemen: Metropolitan, Amran, Aden, Taiz, Al-Hodeida, Hajjah, Ibb, Dhamar, Hadramout and Mareb. The study population was a cohort of smear-positive pulmonary TB (PTB) patients registered for DOTS-based treatment between July 2007 and June 2008. Patients who had completed treatment, were considered cured and were aged ≥ 15 years were included as subjects, while all patients with smear-negative PTB and extra-pulmonary TB (EPTB), children aged <15 years and adult patients receiving other treatment regimens were excluded.

Sampling

The calculation of the sample size for determining factors contributing to relapse was based on a balanced design for simple logistic regression with a binary covariate (X).⁶ In this method, the proportion (B) of the sample ($X = 1$) was assumed to be 0.5. The event rates P_1 and P_2 are 0.05 ($X = 0$) and 0.1 ($X = 1$), respectively. The power of the study was set at 80%, while the two-tailed type I error was assumed to be 5%. The sample size required to detect a change in probability ($Y = 1$) from a baseline value of 0.05 to 0.1 was 862 patients. Adjusting for the variance inflation factor, a total sample size of 880 was needed for multiple logistic regression. Based on the required sample size and the number of patients available according to the previous years' statistics, it was decided that recruitment of all patients within the timeframe July 2007 to June 2008 would provide an adequate sample size.

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KEY WORDS

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Data collection

In the present study, data collection included two main phases: interviewing the participants at the end of the 2-month intensive phase of treatment, and reviewing their medical cards and TB registers at the end of treatment. Patients who were not available for interview during the first visit were interviewed during the next visit. All interviews were conducted by interviewers who were separately trained for this purpose.

We used a pilot test questionnaire and collected demographic, socio-economic and co-morbidity data in the initial phase. Along with the questionnaire, two forms were also used for data collection: the first to collect data from the TB patient cards (adequacy of the treatment regimen, correct doses throughout the treatment period, proportion of prescribed doses actually taken, initial sputum smear status, days missed, weight gain, presence of smear-positive results at the end of the intensive phase and treatment outcome), while the second was used to collect data from the TB registers (adequacy of treatment regimen, initial sputum smear status, smear-positive results at the end of the intensive phase and treatment outcome). Both forms were used to validate each other. Data on cavitation were gathered from the patients' X-ray films.

To avoid interviewer bias, the interviewers were not associated with the TB control health services. Interviews with participants took place in a private room at the target health centre to avoid response bias. Double entry of data by two different persons using EpiData software (Version 6.04, EpiData Association, Odense, Denmark) was conducted to validate data entry. Inconsistencies were checked against raw data.

Definitions

For dependent variables, standard international definitions were used to define treatment outcomes.⁷ We defined relapse as a patient who had successfully completed treatment and was declared cured under the programme and then was diagnosed again with bacteriologically positive (smear/culture) TB.

For independent variables, diabetics were defined as patients who were diagnosed with diabetes and used anti-diabetic drugs.⁸ Patients who habitually chewed and were currently chewing khat (*Catha edulis*, whose leaves are chewed for their stimulating effect in Yemen and in the Horn of Africa) were considered khat chewers. Patients who habitually smoked and were currently smoking were considered smokers. An unemployed individual was a person with no source of income and relied on family to meet all needs. Patient non-adherence was defined as taking <80% of prescribed doses (usually 56 doses during the intensive phase and 168 during the continuation phase),⁹ and/or missing at least 1 month over the entire anti-tuberculosis treatment period.¹⁰ Cavitation was defined as the formation of cavities in the lung as a result of TB; these could be single or multiple cavities, usually with thick walls with irregular margins; in the cavity there might be a small quantity of fluid, visualised as an air-fluid level, usually healing as a linear or fibrotic lesion.¹¹

Ethics

The research was approved by the Ethics Committee of Medical Research in the Ministry of Public Health and Population. Written consent was obtained from the patients.

Statistical analysis

Descriptive and inferential statistics were used in the present study. The association between outcome variables and independent variables was investigated using logistic regression. Multi-

variate logistic regression analysis was performed using SPSS for those risk factors that were found significant in the univariate analysis ($P < 0.1$) to identify independent risk factors for relapse. For the multivariate analysis, $P < 0.05$ was considered statistically significant.

RESULTS

The cohort of new smear-positive PTB cases registered for treatment from July 2007 to June 2008 consisted of 955 patients (Figure 1). Of these, 838 (87.8%) completed the questionnaire. Among the patients interviewed ($n = 838$), only 814 were identified for follow-up. During follow-up, 1.9% ($n = 16$) died and 2.9% ($n = 24$) were lost, giving a final cohort of 774 patients. By the end of the follow-up period, a total of 44 cases who relapsed within 12 months after completion of treatment were identified from the TB register. Accordingly, a total of 176 controls were randomly selected from among those who had not relapsed ($n = 730$). The baseline characteristics of the investigated sample ($n = 220$) are described in Table 1. The relapse rate in this study was 5.7% (44/774); the mean time to relapse was 6.6 months (± 3.2 standard deviation, SD). Twenty cases (45.5%) relapsed within the first 6 months of the follow-up period, while 24 (54.5%) relapsed within the following 6 months.

In the present study, univariate analysis showed that male sex, illiteracy, unemployment, smoking >20 cigarettes per day and non-adherence during the continuation phase were associated with an increased risk of relapse. For disease-related factors, the trend of risk of relapse was high among patients with cavitation, those who had lost $\geq 10\%$ body weight and those with a body mass index ≤ 18.5 kg/m². Diabetics, non-adherent patients and

FIGURE Study flow diagram

TABLE 1 Baseline characteristics of the study sample (N = 220)

Variable	Total n (%)	Cases n (%)	Controls n (%)	P value
Sex				
Female	92 (42)	12 (27)	80 (45)	0.029*
Male	128 (58)	32 (73)	96 (55)	
Age, years				
≥45	25 (11)	5 (11)	20 (11)	NS
<45	195 (89)	39 (89)	156 (89)	
Literacy				
Literate	139 (63)	20 (45)	119 (68)	0.006*
Illiterate	81 (37)	24 (55)	57 (32)	
Marital status				
Married	133 (61)	29 (66)	104 (59)	NS
Unmarried	87 (39)	15 (34)	72 (41)	
Employment				
Employed	91 (41)	11 (25)	80 (45)	0.014*
Unemployed	129 (59)	33 (75)	96 (55)	
Smoking				
No	179 (81)	34 (77)	145 (82)	NS
Yes	41 (19)	10 (23)	31 (18)	
Number of cigarettes				
≤20	210 (95)	38 (86)	172 (98)	0.005†
>20	10 (5)	6 (14)	4 (2)	
Khat chewing				
No	104 (47)	16 (36)	88 (50)	NS
Yes	116 (53)	28 (64)	88 (50)	
Cavitation				
No	151 (69)	16 (36)	135 (77)	<0.05*
Yes	69 (31)	28 (64)	41 (23)	
Took ≥80% of the prescribed doses				
Yes	211 (96)	36 (82)	175 (99)	<0.05†
No	9 (4)	8 (18)	1 (1)	
Missed at least one month of treatment				
No	166 (75)	20 (45)	146 (83)	<0.05*
Yes	54 (25)	24 (55)	30 (17)	
Diabetes				
No	199 (90)	35 (79)	164 (93)	0.010†
Yes	21 (10)	9 (21)	12 (7)	

*P = Pearson χ^2 .

†P = Fisher's exact test.

NS = not significant.

those who gained ≤5% body weight were also at a higher risk of relapse compared with their reference groups. In the multivariate logistic regression analysis, factors that remained independently associated with relapse were unemployment (adjusted odds ratio [aOR] 5.80), number of cigarettes smoked per day (aOR 9.37), presence of cavitation (aOR 6.10), weight gain (aOR 3.14), weight loss (aOR 7.21), non-adherence during the continuation phase (aOR 25.67) and diabetes (aOR 11.47). Table 2 shows the findings of the logistic regression analysis.

DISCUSSION

TB relapse can occur due to endogenous reactivation or exogenous re-infection,¹² conditions that are clinically indistinguishable¹³ but can be differentiated by genotyping techniques.^{12–14} In areas of low TB incidence, relapse is usually due to endogenous reactivation.^{15–17} In areas of high TB incidence, however, the incidence of relapse attributed to re-infection can reach 75%.^{12,18,19} Yemen is a low TB incidence country, with an estimated rate of 25 cases/100 000.¹ Thus, recurrent TB is expected to be due to endogenous

reactivation of the initial strain of *Mycobacterium tuberculosis* rather than to exogenous re-infection.

Our research measured the risks associated with a variety of factors and relapse of TB. A higher risk of relapse was independently associated with unemployment, non-adherence, smoking (number of cigarettes smoked per day), presence of cavitations, weight loss, weight gain and diabetes. Our study showed that unemployment had a significant effect on TB relapse; this may be due to the fact that unemployed patients were more likely to be khat chewers or to have cavitory disease. This was not in agreement with the findings of other researchers.^{20,21} Khat increases the desire to smoke tobacco and causes a lack of appetite, resulting in malnutrition.²²

The findings of this study underscored the importance of adherence to ensure higher cure rates without relapse. Patients who took their treatment irregularly were at higher risk of relapse; this finding was in contrast with previous literature.²³ Although our analysis showed a wide confidence interval, which could have made the results inconclusive, non-adherence during the continuation phase was expected to be a risk factor for relapse in Yemen, where the continuation phase is self-administered.

This study showed a significant association between TB relapse and smoking. Comparable findings have been reported in the literature.^{17,20,21,24} The mechanism proposed to explain the association between smoking and TB is the neutralisation of tumour necrosis factor alpha (TNF- α) by substances found in tobacco.²⁵ The reduction in TNF- α and nitric acid, which play a role in containing the intracellular growth of *M. tuberculosis*, may be explained by the high level of iron in the bronchoalveolar macrophages of smokers.²⁶ This mechanism may also be the reason behind the development of relapse.

A strongly significant effect of cavitation on relapse has also been shown in our study, corroborating the findings of other studies.^{17,23,27} The association between cavitation and relapse could be attributed to poor drug penetration into the devascularised cavities or the surrounding fibrotic tissue.²⁷ Our study shows that weight gain is strongly associated with TB relapse, supporting the findings of Khan et al.²⁸ However, weight loss was also significantly associated with increased risk for relapse, corroborating the findings of Benator et al.²⁷

The positive association between diabetes and TB has been reported previously.^{8,23,29} We confirm that diabetes is an important factor for recurrent TB. However, the present findings are inconsistent with those of a Brazilian study.³⁰ The existence of a significant association between diabetes and relapse in our study may be due to malabsorption of anti-tuberculosis drugs among diabetic patients due to hyperglycaemia,²⁹ which may interfere with achieving adequate tissue levels of anti-tuberculosis drugs. The degree of hyperglycaemia has a distinct influence on the microbicidal function of macrophages and CD4⁺ cells.³¹

Our findings have several implications for the NTCP. First, there is a need for action to help unemployed patients. Offering extra services, including free services for the unemployed, and extension of opening hours for those who cannot keep their medical appointments due to work, could be expected to lead to a reduction in non-adherence and thus a reduction in risk of relapse. The study findings suggest that non-adherence to treatment is a significant risk factor for relapse. The relapse rate under the NTCP can be reduced by ensuring that patients take their treatment on a regular basis. Reinforcing the implementation of the DOTS strategy, a method widely acknowledged to reduce rates of treatment failure, drug resistance and relapse,³² and the clinicians' assessment of patient adherence must remain integral components of

TABLE 2 Logistic regression analysis (*N* = 220)

	Total <i>n</i>	Relapse <i>n</i> (%)	Univariate OR (95%CI)	<i>P</i> value	Multivariate aOR (95%CI)
Demographic factors					
Sex					
Female (reference)	92	12 (13)			
Male	128	32 (25)	2.2 (1.1–4.6)	0.03*	
Age, years					
≥45 (reference)	25	5 (20)			
<45	195	39 (20)	1.0 (0.9–1.0)	NS	
Literacy					
Literate (reference)	139	20 (14)			
Illiterate	81	24 (30)	2.5 (1.3–4.9)	0.007*	
Marital status					
Married (reference)	133	29 (22)			
Unmarried	87	15 (17)	1.3 (0.7–2.7)	NS	
Socioeconomic factors					
Employment					
Employed (reference)	91	11 (11)			
Unemployed	129	33 (26)	2.5 (1.2–5.3)	0.02*	5.8 (1.7–19.6)
Smoking					
No (reference)	179	34 (19)			
Yes	41	10 (24)	1.4 (0.6–3.1)	NS	
Number of cigarettes					
≤20 (reference)	210	38 (18)			
>20	10	6 (60)	6.8 (1.8–25.2)	0.004*	9.4 (1.1–83.9)
Khat chewing					
No (reference)	104	16 (15)			
Yes	116	28 (24)	1.8 (0.9–3.5)	NS	
Treatment-related factors					
Adequate regimen					
Yes (reference)	219	43 (20)			
No	1	1 (100)	Undefined	NS	
Correct dose in IP					
Yes (reference)	216	42 (19)			
No	4	2 (50)	4.1 (0.6–30.3)	NS	
Correct dose in CP					
Yes (reference)	216	43 (20)			
No	4	2 (25)	1.3 (0.1–13.2)	NS	
Took ≥80% of prescribed doses in IP					
Yes (reference)	218	43 (20)			
No	2	1 (50)	4.1 (0.3–66.4)	NS	
Took ≥80% of prescribed doses in CP					
Yes (reference)	211	36 (17)			
No	9	8 (89)	38.9 (4.7–320.6)	0.001*	25.7 (2.2–297.9)
Disease factors					
Sputum smear status					
One + (reference)	162	33 (20)			
Two ++	36	4 (11)	0.5 (0.2–1.5)	NS	
Three +++	22	7 (32)	1.8 (0.7–4.8)	NS	
Cavitation					
No (reference)	151	16 (11)			
Yes	69	28 (41)	5.8 (2.8–11.7)	<0.001*	6.1 (2.2–16.9)
Weight loss (<i>n</i> = 217)					
<10% (reference)	141	15 (11)			
≥10%	76	29 (38)	5.2 (2.6–10.5)	<0.001*	7.2 (2.4–21.9)
BMI (<i>n</i> = 217)					
>18.5 kg/m ² (reference)	149	21 (14)			
≤18.5 kg/m ²	68	23 (34)	3.1 (1.6–6.2)	0.001*	
Diabetes					
No (reference)	199	35 (18)			
Yes	21	9 (43)	3.5 (1.4–8.9)	0.009*	11.5 (2.6–50.7)
Factors evaluated after 2–3 months of treatment					
Positivity at 2nd month					
Negative (reference)	207	39 (19)			
Positive	13	5 (39)	2.7 (0.8–8.7)	NS	
Weight gain					
>5% (reference)	90	11 (12)			
≤5%	130	33 (25)	2.4 (1.2–5.1)	0.019*	3.1 (1.0–9.6)
Missed at least one month of treatment					
No (reference)	166	20 (12)			
Yes	54	24 (44)	5.8 (2.9–11.9)	<0.001*	

*Statistically significant.

OR = odds ratio; CI = confidence interval; aOR = adjusted odds ratio; NS = not significant (*P* > 0.1); IP = intensive phase; CP = continuation phase; BMI = body mass index.

TB control. Social support can help patients overcome structural as well as personal barriers; however, community and family members' attitudes may influence a patient's decision about whether to stop or continue TB treatment. In such circumstances, community-based TB treatment programmes and stronger involvement of local social networks to support TB patients may be justified.³³

Second, it may not be sufficient simply to cure patients to achieve TB control (as cured patients can relapse); it is important for NTCPs to incorporate strategies that reduce the risk of relapse, including smoking cessation support.²¹ Enhancing health education activities in the programme, and drawing attention to the impact of smoking on a patient's health, could be an effective tool for reducing the risk of relapse among cured TB patients. To have far-reaching effects on the population's health, anti-smoking campaigns need to be reinforced.²⁰

Third, and most importantly, the standard treatment regimen containing RMP during the continuation phase was not used in Yemen until recently. In the randomised controlled trial mentioned, the relapse rate for a 6-month regimen containing RMP throughout (2RHZE/4HR) was half that for 2RHZE/6HE (5%).³⁴ Therefore, changing from the current standard regimen to one with RMP in the continuation phase could reduce the relapse rate, especially among patients with cavitary TB, where a high proportion of surviving persisters are expected. RMP is the pivotal drug due to its rapid sterilising action.³⁵ The probability of eradicating persisters is thus largely determined by the total number of doses of RMP, which can be increased by modifying dosing frequency, treatment duration, or both. A study in Hong Kong²³ showed that extension of both the intensive phase and overall treatment by $\geq 50\%$ protected against relapse. Based on estimates of relapse rates in that study,²³ the standard thrice-weekly regimen with fewer administered doses might still be cost-effective in the absence of cavitation. However, among patients with positive pre-treatment culture and cavitation, meaningful reductions in the relapse rate could be achieved by a daily regimen, and the risk might be further reduced by prolonging treatment. Based on previous evidence, it can be recommended to use RMP-based regimens in the treatment of cavitary TB in Yemen's NTCP.

Fourth, the study findings showed a significant association between diabetes and TB relapse. To reduce the eventuality of this association, the WHO recently recommended bi-directional screening in patients with TB and diabetes. Based on this recommendation, all diabetes patients should be counselled on the risk of TB and screened for TB on a regular basis. Similarly, TB patients should be screened for diabetes to reduce the occurrence of relapse among cured patients.

Fifth, the study showed that both weight loss and weight gain had a significant effect on relapse. Weight gain of $<5\%$ could be a marker of increased TB disease activity and/or poor response to treatment. These findings imply that for patients who gain $\leq 5\%$ weight, there is a need for drug susceptibility testing as well as reinforcement of the DOTS strategy. The very high relapse rate (46.8%) among underweight patients with $\leq 5\%$ weight gain during the 2-month intensive phase raises the possibility that such patients should receive treatment that is either more intensive or of longer duration.²⁸

The main strengths of this study are its prospective design, the large sample size and active follow-up for relapse for a year after treatment completion. Unlike some previous cohort studies that included only high-risk populations, such as human immunodeficiency virus (HIV) co-infected TB patients or the homeless, this study was conducted in a general TB population. Despite these positive points, our study has several limitations. First, approxi-

mately 12% of the subjects were excluded due to primary default, transfer out, death, refusal to respond and the use of other treatment regimens. Second, distinguishing between relapse and reinfection requires molecular strain typing of both the initial and the recurrent *M. tuberculosis* isolates, data that were unavailable for the subjects in this study. Third, the potential role of HIV was not investigated due to ethical, political and practical considerations. In addition, screening for HIV among TB patients is not a routine activity in the NTCP, and the proportion of TB-HIV patients seems to be low. Based on a recent survey completed on TB-HIV co-infection among 900 TB cases, there were six HIV-positive cases, indicating low HIV incidence ($<1\%$).^{1,2}

CONCLUSION

The relapse rate can be reduced by ensuring that patients take their treatment regularly and are counselled effectively on quitting smoking. Reinforcing the application of the DOTS strategy and strengthening anti-smoking campaigns are important issues. Action to help unemployed patients should be adopted by the government, including a free of charge service, the extension of service hours and creation of new job opportunities. The use of rifampicin-based regimens in the treatment of cavitary TB and bi-directional screening in patients with TB and diabetes are recommended. Additional studies are warranted to identify cost-effective interventions that will reduce the risk of relapse.

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Contexte : Le Programme national de lutte contre la tuberculose (TB) du Yemen.

Objectif : Identifier les facteurs de risque en association avec la rechute de TB.

Méthodes : Dans une étude cas-contrôle prospective nichée, les cas de rechute ont été recrutés à partir d'une cohorte de patients tuberculeux pulmonaires enregistrés entre juillet 2007 et juin 2008. On a sélectionné au hasard quatre contrôles par cas à partir d'une liste de patients sans rechute. Pour le recueil des données, on a utilisé trois formulaires couvrant les interviews des participants et la révision de leurs dossiers médicaux et des registres TB. On a exécuté une analyse de régression logistique multivariée pour identifier les facteurs de risque indépendants pour la rechute.

Résultats : On a noté un taux de rechute de 5,7%. L'analyse de ré-

gression logistique multivariée a démontré que le chômage, le tabagisme, la présence de lésions cavitaires, le gain de poids, la perte de poids, la non-adhésion à la phase de continuation et le diabète sont associés de manière significative à la rechute ($P < 0,05$).

Conclusion : Le taux de rechute peut être réduit en s'assurant que les patients prennent leur traitement régulièrement et en conseillant avec efficience l'arrêt du tabac. La consolidation de l'application de la stratégie DOTS et le renforcement des campagnes anti-tabac sont des problèmes importants. On devrait adopter un programme d'action pour aider les chômeurs en proposant une gratuité des soins et la création de nouvelles opportunités d'emploi. On recommande l'utilisation de régimes basés sur la rifampicine pour le traitement de la tuberculose cavitaire ainsi qu'un dépistage bidirectionnel des patients pour la TB et le diabète.

Marco de referencia: El Programa Nacional de control de la Tuberculosis (TB) de Yemen.

Objetivo: Determinar los factores de riesgo asociados con la recaída de la TB.

Método: Fue este un estudio prospectivo, anidado, de casos y testigos. Se incluyeron los casos de recaída de una cohorte de pacientes con TB pulmonar registrados entre julio del 2007 y junio del 2008. Se escogieron de manera aleatoria cuatro testigos por cada caso de una lista de pacientes sin recaída. Se utilizaron tres formularios en la recogida de los datos que comportaban una entrevista a los participantes, el examen de las tarjetas de tratamiento y los registros de TB. Mediante un análisis de regresión logística se definieron los factores de riesgo independientes asociados con la recaída.

Resultados: Se observó una tasa de recaída de 5,7%. El análisis de regresión logística puso en evidencia que el desempleo, el tabaquismo,

la presencia de cavernas en el pulmón, la ganancia de peso, la pérdida de peso, el incumplimiento terapéutico durante la fase de tratamiento continuo y la presencia de diabetes se asociaban de manera significativa con la posibilidad de recaída ($P < 0,05$).

Conclusión: La tasa de recaída de la TB se puede disminuir, al procurar que los pacientes tomen los medicamentos de manera regular y aconsejándoles de manera eficaz que abandonen el tabaquismo. El refuerzo de la aplicación de la estrategia DOTS y el fortalecimiento de las campañas contra el tabaco constituyen aspectos importantes. Se deben tomar las medidas apropiadas de ayuda a los pacientes desempleados, entre ellas la prestación de servicios sin costo alguno y la creación de nuevas oportunidades de trabajo. Se recomienda el uso de regímenes basados en rifampicina en el tratamiento de los casos de TB con presencia de cavernas y la instauración de una detección sistemática bidireccional en los pacientes con TB y diabetes.