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Increased risk of pulmonary tuberculosis in patients with previous non-tuberculous mycobacterial disease

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SUMMARY

OBJECTIVE: To investigate whether or not there is an increased risk of pulmonary tuberculosis (PTB) after non-tuberculous mycobacterial (NTM) disease.

DESIGN: A retrospective cohort study of 212 NTM patients and 4240 control cases.

RESULTS: Patients with previous NTM disease had a significantly higher incidence of PTB than controls (incidence rate ratio [IRR] 14.74, 95%CI 8.71–24.94, $P < 0.0001$). Cox's proportional hazards analysis yielded an adjusted hazards ratio (aHR) of 10.15 (95%CI 5.67–18.17, $P < 0.05$) for NTM-associated PTB. The majority of the PTB cases (17/23, 73.9%) were diagnosed within 6 months after the diagnosis of NTM disease. Older age (≥65 years, aHR 4.45, 95%CI 1.94–10.22, $P < 0.05$), male sex (aHR 1.75, 95%CI 1.01–3.13, $P < 0.05$), human immunodeficiency virus (HIV) infection (aHR 12.49, 95%CI 3.20–48.79, $P < 0.05$) and chronic obstructive pulmonary disease (aHR 4.46, 95%CI 2.19–9.10, $P < 0.05$) were independent risk factors for developing PTB after NTM disease. The cumulative incidence of PTB in patients with previous NTM disease was significantly higher than in controls ($P < 0.0001$, Kaplan-Meier analysis). However, there was no significant difference in the survival rates in the two cohorts.

CONCLUSION: Increased PTB prevalence after NTM disease was demonstrated. HIV infection was the greatest independent risk factor for subsequent development of PTB.

KEY WORDS: tuberculosis; NTM disease; human immunodeficiency virus; population-based cohort study

APPROXIMATELY one third of the world's population is infected with *Mycobacterium tuberculosis* (TB),[1] with 8.8 million new cases and 1.4 million deaths worldwide reported in 2010.[2] TB has also contributed the highest number of incident cases to all of reported infectious diseases in Taiwan for decades.[3] From 2002 to 2008, the number of new TB cases in Taiwan declined from 16 758 to 14 265, and TB incidence decreased from 75 to 62 per 100 000 population following the implementation of the DOTS strategy in 2006.[4]

Mycobacteria other than the *Mycobacterium tuberculosis* complex and *M. leprae* are termed non-tuberculous mycobacteria (NTM);[5] these organisms are not always pathogenic when isolated from human samples.[6] NTM infection only began to attract interest following the acquired immunodeficiency syndrome (AIDS) epidemic, and most published reports have come from non-TB-endemic countries.[7] However, the incidence of NTM disease is currently on the rise in both immunocompetent and immunocompromised hosts.[8,9]

The diagnosis of NTM disease is difficult due to the lack of appropriate diagnostics, and the overlapping clinical manifestations caused by TB in TB-endemic regions[10,11] may pose a challenge for DOTS-based programmes. As patients with acid-fast bacilli (AFB) positive on respiratory samples are generally presumed to be infected with TB, they are treated with anti-tuberculosis agents. This means that many patients with NTM disease may receive inappropriate and ineffective empirical anti-tuberculosis treatment.

Individuals with medical conditions that compromise the immune system, including elderly patients, have a higher risk of developing TB, as do those with human immunodeficiency virus (HIV) infection, diabetes, silicosis or cancer, those receiving immunosuppressive treatment, those from low socio-economic backgrounds and those recently infected with TB.[12–14] In addition, increasing evidence has shown that

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advanced age, male sex, malignancy, HIV infection, multidrug-resistant TB (MDR-TB) and mechanical ventilation are risk factors for unfavourable outcomes of anti-tuberculosis treatment.[15–19] As the incidence of NTM disease and clinical NTM and TB co-infection increases, DOTS-based anti-tuberculosis treatment may influence the occurrence and outcome of TB after NTM disease. However, it remains unclear whether previous NTM disease has an important impact on the increase in incidence or poor treatment outcomes of subsequent pulmonary TB (PTB).

This study aimed to investigate the relationship between the incidence and outcome of PTB treatment after NTM disease in Taiwan based on population data.

STUDY POPULATION AND METHODS

Data sources

Taiwan launched a single-payer National Health Insurance (NHI) programme on 1 March 1995; NHI databases cover nearly all of the Taiwanese population (coverage rate >98% in 2009). Data used in this study came from the Longitudinal Health Insurance Database 2000 (LHID2000), which contains all claims data from 1996 to 2009 of one million beneficiaries randomly selected in 2000, representing approximately 5% of all enrollees in Taiwan. LHID2000 provides encrypted patient identification numbers, sex, date of birth, dates of admission and discharge, International Classification of Diseases Ninth Revision Clinical Modification (ICD-9-CM) codes of diagnoses and procedures, details of prescriptions, records from the Catastrophic Illness Patient Database, and costs covered and paid for by the NHI.

Because the identification numbers of all individuals in the LHID2000 were encrypted to protect their privacy for research purposes, the study was exempt from full review by the institutional review board of the Chi Mei Medical Center, Tainan, Taiwan.

Study population

Our retrospective cohort study from 1 January 1999 to 31 December 2008 was based on ambulatory care and in-patient discharge records. NTM disease was defined by an ICD-9-CM-compatible code (031) in the primary diagnosis. Individuals with PTB diagnosed before NTM disease were excluded. A total of 212 NTM patients were included in the study.

Comparison group patients (n = 4240, 20 subjects for every NTM patient), matched by sex, age and index date, were randomly selected from the data set. The index date for NTM subjects was the date of first registration, while the index date for the comparison group was created by matching the date of the NTM subject's index date. Patients diagnosed with TB before the index date were excluded.

Each patient was followed up to determine the incidence of PTB (ICD-9 code 010-012) until the end of 2009 or censored if dead. PTB incidence rates, incidence rate ratios (IRRs) and hazard ratios (HRs) were analysed. Comorbidities were defined based on the claims data, and included stroke (ICD-9-CM codes 430–438), diabetes mellitus (ICD-9-CM code 250), liver cirrhosis (ICD-9-CM codes 5712, 5715, 5716 and 7895), chronic kidney disease (ICD-9-CM codes 582, 583, 585, 586, 588), HIV (ICD-9-CM codes 042–044) and chronic obstructive pulmonary disease (COPD; ICD-9-CM codes 491, 492 and 496). We included these comorbid conditions in our analysis if the condition occurred either in the in-patient setting or in two or more ambulatory care claims coded 12 months before the index medical care date.

Statistical analysis

Pearson's χ^2 tests were used to compare the NTM group and the non-NTM group in terms of demographic characteristics and comorbidities. Fisher's exact test was performed if 25% of the cells had expected counts of <5 in categorical variables. The difference in age between the two groups was compared using Student's t-test. The risk of PTB was compared between the two cohorts by estimating the IRR using Poisson regression. The risk of developing PTB associated with comorbidities was estimated using Cox's proportional hazard models. Kaplan-Meier analysis was used to calculate the cumulative incidence rates of PTB in the two cohorts, and the log-rank test was used to analyse survival curves. Kaplan-Meier analysis was also used to estimate the mortality rates of PTB patients in the two cohorts. All analyses were performed using SAS software, version 9.3 (Statistical Analysis Software Institute, Cary, NC, USA); the statistical significance level was set at two-sided $P < 0.05$.

RESULTS

Demographic data

Over the 11 years of the study, between 1999 and 2009, 212 NTM patients and 4240 age- and sex-matched controls were recruited from one million beneficiaries. The annual incidence of NTM disease was thus 1.9 per 100 000 person-years (py). Individual matching resulted in comparable distributions of cases and controls by age and sex.

As shown in Table 1, the two groups were similar in sex and age distribution, with a mean age of 43.6 years. We classified these patients into four age subgroups: ⩽35, 35–49, 50–64 and ⩾65 years. NTM patients were more likely to have a higher prevalence of stroke (8.0% vs. 5.3%, $P < 0.0001$), liver cirrhosis (2.8% vs. 0.7%, $P = 0.0048$), HIV infection (3.8% vs. 0.02%, $P < 0.0001$) and COPD (10.4% vs. 2.2%, $P < 0.0001$) than controls.

Pulmonary tuberculosis incidence after non-tuberculous mycobacterial disease

Of the 4452 patients, 58 were diagnosed with PTB during the follow-up period: 23/212 (18.5%) in the

Table 1 Demographic characteristics and comorbidities for NTM patients and controls

	NTM patients (n = 212) n (%)	Controls (n = 4240) n (%)	P value
Age, mean ± SD	43.62 ± 22.34	43.62 ± 22.29	0.9999
Age, years			
0–35	81 (38.21)	1620 (38.21)	1.0000
35–49	44 (20.75)	880 (20.75)	
50–64	41 (19.34)	820 (19.34)	
⩾65	46 (21.70)	920 (21.70)	
Sex			
Female	94 (44.34)	1880 (44.34)	1.0000
Male	118 (55.66)	2360 (55.66)	
Baseline comorbidity			
Stroke			
Yes	17 (8.02)	107 (2.52)	<0.0001
No	195 (91.98)	4133 (97.48)	
Chronic kidney disease			
Yes	4 (1.89)	55 (1.30)	0.4638*
No	208 (98.11)	4185 (98.70)	
Diabetes mellitus			
Yes	17 (8.02)	259 (6.11)	0.2603
No	195 (91.98)	3981 (93.89)	
Liver cirrhosis			
Yes	6 (2.83)	28 (0.66)	0.0048*
No	206 (97.17)	4212 (99.34)	
HIV			
Yes	8 (3.77)	1 (0.02)	<0.0001*
No	204 (96.23)	4239 (99.98)	
COPD			
Yes	22 (10.38)	92 (2.17)	<0.0001
No	190 (89.62)	4148 (97.83)	

*Fisher's exact test.
NTM = non-tuberculous mycobacteria; SD = standard deviation; HIV = human immunodeficiency virus; COPD = chronic obstructive pulmonary disease.

NTM group and 35/4240 (0.8%) among the controls (Table 2). The PTB incidence rate was respectively 24.32 and 1.65/1000 py for the NTM and control groups. NTM patients had significantly higher PTB incidence than the control group (IRR 14.74, 95% confidence interval [CI] 8.71–24.94, $P < 0.0001$); the PTB incidence rates in the NTM group, classified by age, sex and follow-up month, were also all higher than in the control group. The oldest age group (⩾65 years) in the NTM group had the highest incidence of PTB (incidence rate [IR] 68.83/1000 py), but patients aged 0–35 years had the highest IRR (26.23, 95%CI 8.01–85.94, $P < 0.0001$). Male patients showed a higher risk of PTB than female patients. NTM patients with HIV infection or COPD had a higher PTB IR (157.89 vs. 21.59 and 121.07 vs. 18.97, respectively) than those without HIV infection or COPD. However, among individuals without HIV comorbidity, NTM patients had a significantly higher IRR (13.07, 95%CI 7.55–22.66, $P < 0.0001$) for developing PTB than controls. Furthermore, among individuals without COPD, NTM patients had a significantly higher IRR (14.67, 95%CI 7.99–26.916, $P < 0.0001$) for developing PTB than controls (Table 2). The PTB incidence rate in the NTM group by follow-up time was very high in the first 2 months (IR 330.03/1000 py), then it decreased to respectively 94.97, 21.08 and 5.30 in 2–6 months, 6–12 months and >12 months. The analysis of follow-up duration also showed that the risk of PTB in NTM patients was highest in the first 2 months (IRR 114.18, 95%CI

Table 2 Risk of pulmonary TB in previous NTM patients and controls

	NTM patients				Controls					
Characteristic	Total n	TB n	py	Incidence rate/ 1000 py	Total n	TB n	py	Incidence rate/ 1000 py	IRR (95%CI)	P value
All	212	23	945.8	24.32	4240	35	21 210.8	1.65	14.74 (8.71–24.94)	<0.0001
Age, years										
0–35	81	6	429.3	13.97	1620	5	9 382.2	0.53	26.23 (8.01–85.94)	<0.0001
35–49	44	2	215.7	9.27	880	4	4 622.7	0.87	10.71 (1.96–58.50)	0.0062
50–64	41	6	170.0	35.29	820	7	3 836.5	1.82	19.34 (6.45–57.54)	<0.0001
⩾65	46	9	130.8	68.83	920	19	3 369.5	5.64	12.21 (5.52–26.98)	<0.0001
Sex										
Male	118	18	483.7	37.21	2360	22	11 691.9	1.88	19.78 (10.61–36.87)	<0.0001
Female	94	5	462.1	10.82	1880	13	9 518.8	1.37	7.92 (2.82–22.22)	<0.0001
Comorbidities										
HIV										
Yes	8	3	19.2	157.89	1	0	4.9	0	—	—
No	204	20	926.5	21.59	4239	35	21 205.9	1.65	13.07 (7.55–22.66)	<0.0001
COPD										
Yes	22	6	49.6	121.07	92	8	335.0	23.88	5.07 (1.76–14.61)	0.0026
No	190	17	896.2	18.97	4148	27	20 875.8	1.29	14.67 (7.99–26.91)	<0.0001
Follow-up time, months										
<2	212	11	33.3	330.03	4240	2	696.0	2.87	114.8 (25.46–518.1)	<0.0001
2–6	198	6	63.2	94.97	4232	4	1 389.8	2.88	32.99 (9.31–116.9)	<0.0001
6–12	188	2	94.9	21.08	4224	4	2 139.0	1.87	11.27 (2.06–61.54)	0.0052
⩾12	186	4	754.4	5.30	4207	25	17.0	1.47	3.06 (1.25–10.35)	0.0173

TB = tuberculosis; NTM = non-tuberculous mycobacteria; py = person-years; IRR = incidence rate ratio; CI = confidence interval; HIV = human immunodeficiency virus; COPD = chronic obstructive pulmonary disease.

25.46–518.1, $P < 0.0001$), and gradually declined to an IRR of 3.06 (95%CI 1.25–10.35, $P = 0.0173$) after 12 months.

Multivariate analysis for the prediction of pulmonary tuberculosis development

Table 3 shows the crude and adjusted hazard ratios (HRs) using Cox's proportional hazards analysis for PTB during the follow-up period by cohort for the total sample. It yielded a crude HR of 14.47 (95%CI 8.55–24.49, $P < 0.05$) and an adjusted HR for PTB of 10.15 (95%CI 5.67–18.17, $P < 0.05$) associated with NTM disease. The HR increased with age. Male sex (adjusted HR [aHR] 1.75, 95%CI 1.01–3.13, $P < 0.05$) and comorbidity with HIV positivity (aHR 12.49, 95%CI 3.20–48.79, $P < 0.05$) and COPD (aHR 4.46, 95%CI 2.19–9.10, $P < 0.05$) were independent risk factors for PTB.

Cumulative incidence and survival rates in pulmonary tuberculosis patients

Kaplan-Meier estimates of the cumulative incidence of PTB in NTM patients and controls are shown in the Figure. The cumulative incidence of PTB in NTM patients was significantly higher than in controls ($P < 0.0001$). Kaplan-Meier analysis was used to calculate the survival rates of TB patients in the two cohorts after TB diagnosis ($P = 0.9970$); no significant differences were observed between the two cohorts.

Table 3 Crude and adjusted HRs of patients who developed pulmonary tuberculosis after NTM disease

Cohort	Crude HR (95%CI)	Adjusted HR (95%CI)
NTM		
Yes	14.47 (8.55–24.49)*	10.15 (5.67–18.17)*
No	1.00	1.00
Age, years		
0–35	1.00	1.00
35–49	1.05 (0.39–2.84)	1.21 (0.43–3.37)
50–64	2.56 (1.15–5.72)*	2.82 (1.20–6.62)*
⩾65	5.55 (2.75–11.23)*	4.45 (1.94–10.22)*
Sex		
Female	1.00	1.00
Male	1.85 (1.05–3.23)*	1.75 (1.01–3.13)*
Stroke		
Yes	5.70 (2.58–12.59)*	1.55 (0.67–3.57)
No	1.00	1.00
Chronic kidney disease		
Yes	4.92 (1.54–15.75)*	3.01 (0.86–10.57)
No	1.00	1.00
Diabetes mellitus		
Yes	3.08 (1.51–6.27)*	1.34 (0.64–2.82)
No	1.00	1.00
Liver cirrhosis		
Yes	2.81 (0.39–20.31)	0.35 (0.04–3.05)
No	1.00	1.00
HIV		
Yes	36.00 (11.24–115.29)*	12.49 (3.20–48.79)*
No	1.00	1.00
COPD		
Yes	14.51 (7.92–26.56)*	4.46 (2.19–9.10)*
No	1.00	1.00

*$P < 0.05$.
HR = hazard ratio; NTM = non-tuberculous mycobacteria; CI = confidence interval; HIV = human immunodeficiency virus; COPD = chronic obstructive pulmonary disease.

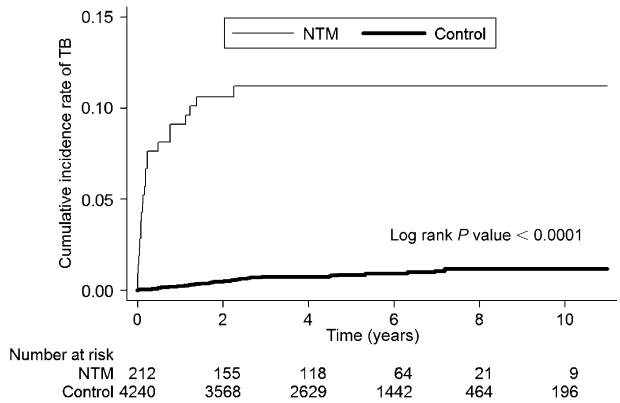

Figure Kaplan-Meier analysis was used to calculate the cumulative incidence rates of pulmonary TB in the two cohorts; the log-rank test was used to analyse the differences between the two curves.

DISCUSSION

To our knowledge, this is the first study to investigate the causal association between NTM disease and PTB in a nationwide cohort of patients. We found that after taking confounding factors into account, previous NTM disease was associated with a 14.5-fold greater risk (aHR 10.15) of later developing PTB, and that the magnitude of association was highest for HIV patients (aHR 12.49).

Overall incidence rates of NTM disease have increased from 1.0–1.8 to 3.2–7.2/100 000 in the past decade.[8,20,21] In Taiwan, Lai et al. reported an incidence rate of NTM disease of 2.23/100 000 outpatients[22] and 4.3/100 000 elderly patients (aged ⩾65 years), whereas their NTM colonisation rate was 15.8 in 2008.[23] Our results demonstrate a mean annual incidence of NTM disease of 1.9/100 000, in line with previous reports.

As PTB is a major underlying disease in patients with NTM lung disease,[24,25] reverse causality was possible in this study. A diagnosis of TB before or on the same day of the diagnosis of NTM disease was thus excluded to avoid the possibility of reverse causality. The follow-up year after the diagnosis of NTM disease played an important role in understanding the causal relationship. The majority of the PTB patients (17/23 cases, 73.9%) were diagnosed within 6 months after the diagnosis of NTM disease, indicating the common occurrence of NTM and PTB co-infection: the co-existence of TB and NTM disease is therefore not uncommon,[6,10,26,27] Jun et al. reported the isolation of NTM from respiratory cultures among 7.1% of patients undergoing anti-tuberculosis treatment,

and the co-existence of NTM and PTB disease should be considered in patients harbouring relatively virulent NTM species.[6,10,26] However, as 11/23 patients (47.8%) with PTB were diagnosed within 2 months, delays in the diagnosis of PTB in this group cannot be excluded as it can take several weeks for cultures to become positive for TB isolates when rapidly growing mycobacteria are also present.[26,28] Huang et al. reported rapidly growing mycobacteria in 50.6% of NTM isolates from PTB patients.[26] Nevertheless, the risk of developing PTB during the two follow-up intervals of 6–12 months and >12 months was also significantly increased, even when concurrent NTM and PTB disease was not likely. Our results demonstrate that NTM patients without HIV infection or COPD had significantly higher IRRs (13.07 and 14.67, respectively) for developing PTB than controls without HIV or COPD (Table 2). This positive correlation indicates that NTM disease is an important risk factor for the development of PTB.

Among NTM patients, those aged >50 years, male, with HIV infection or COPD had high odds of developing PTB using multivariate analysis. Aging, which is related to progressive immune dysregulation such as the reduction in CD8+ T-cells and a decline in T-cell proliferation,[29,30] may thus contribute to the risk of developing PTB in the NTM group. In addition, HIV infection represents a high risk for predisposition to PTB and NTM.[24,31] The risk of disease due to NTM was particularly high in patients with a CD4+ lymphocyte count of <100 cells/ml.[24] Males were more likely to develop HIV infection and COPD. In addition, COPD patients characterised by older age, chronic smoke inhalation and lung tissue destruction may have poorly functioning innate immune systems, resulting in increased susceptibility to infection by pathogenic and opportunistic organisms.[32,33] In our results, NTM patients aged <35 years (the HIV epidemic age but not the COPD prevalence age) had a higher IRR (26.2 vs. 12.2) of developing PTB than controls aged ⩾65 years. Immunocompromised status may thus play an important role in the development of PTB after NTM infection.

The actual mechanisms responsible for the causal association between NTM and PTB are largely unclear. However, NTM infection is common in patients with structural lung disease,[34–36] acquired morbidity[37] and immunodeficiency,[38] and in those who have recently undergone organ transplantation.[39] These risk factors were also found in patients with TB.[2] Moreover, genetic defects or mutations related to the activation of or response to interleukin 12/interferon-gamma/signal transducers and activators of transcription 1 signalling pathways have been reported to enhance the risk of developing both NTM and TB disease.[40,41] Taken together, impaired immune status may be an important cause of the association between previous NTM disease and increased susceptibility to PTB.

The survival outcome of PTB treatment did not demonstrate significant differences between the two cohorts. A well-run TB treatment programme can result in acceptable cure rates, even in a population with TB-HIV co-infection,[33,34] thus suggesting a favourable outcome for DOTS-based treatment for TB after NTM infection.

Our study had some limitations. First, we identified TB and NTM cases based on the diagnostic codes provided by physicians in the administrative database, and coding errors and misdiagnoses were possible. Second, data on variables associated with both NTM and PTB, such as body mass index, cigarette smoking and alcohol consumption, were not available, allowing for the possibility of residual confounding factors. Third, we were unable to assess adherence to prescribed medications, as drug use data were not obtained from claims databases.

CONCLUSION

Increased prevalence of PTB after NTM disease was confirmed. HIV infection among NTM patients provided the highest independent risk factor for subsequent development of PTB. Avoiding risk factors and reducing NTM infection are thus important strategies for TB control.

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RÉSUMÉ

OBJECTIF : Investiguer dans quelle mesure le risque de tuberculose pulmonaire (TBP) est oui ou non accru après une maladie due aux mycobactéries non tuberculeuses (NTM).

SCHÉMA : On a mené une étude rétrospective de cohorte comportant 212 patients NTM et 4240 cas-contrôle.

RÉSULTATS : Chez les patients avec antécédents de maladie due aux NTM, le taux d'incidence de développement d'une TBP est significativement plus élevé que chez les contrôles (ratio de taux d'incidence [IRR] 14,74 ; IC95% 8,71–24,94 ; $P < 0,0001$). L'analyse des risques proportionnels de Cox a démontré un ratio de risque ajusté (aHR) de 10,15 (IC95% 5,67–18,17 ; $P < 0,05$) de TBP liée à la maladie due aux NTM. La majorité des cas de TBP (17/23, 73,9%) ont été diagnostiqués dans les 6 mois après le diagnostic de maladie due aux NTM. Les facteurs de risque indépendants de développement d'une TBP après une maladie due aux NTM ont été un âge plus avancé (⩾65 ans, aHR 4,45 ; IC95% 1,94–10,22 ; $P < 0,05$), le sexe masculin (aHR 1,75 ; IC95% 1,01–3,13 ; $P < 0,05$), l'infection par le virus de l'immunodéficience humaine (VIH ; aHR 12,49 ; IC95% 3,20–48,79 ; $P < 0,05$), ainsi que la bronchopneumopathie chronique obstructive (aHR 4,46 ; IC95% 2,19–9,10 ; $P < 0,05$). L'incidence cumulative de la TBP chez les patients avec antécédents de maladie due aux NTM a été significativement plus élevée que chez les contrôles ($P < 0,0001$, analyse de Kaplan-Meier). Toutefois, les taux de survie des patients TBP sont similaires dans les deux cohortes.

CONCLUSION : On a démontré une prévalence accrue de la TBP après une maladie due aux NTM. L'infection par le VIH constitue le facteur de risque indépendant le plus élevé d'apparition ultérieure d'une TBP.

RESUMEN

OBJETIVO: Investigar si las enfermedades causadas por micobacterias atípicas (NTM) aumentan el riesgo de contraer la tuberculosis pulmonar (TBP).

MÉTODOS: Fue este un estudio retrospectivo de cohortes en el cual se incluyeron 212 pacientes con NTM y 4240 casos de referencia.

RESULTADOS: Los pacientes con antecedente de enfermedad causada por NTM presentaron una tasa de incidencia de TBP significativamente mayor que los testigos (razón de tasas de incidencia [IRR] 14,74; IC95% 8,71–24,94; $P < 0,0001$). Mediante el modelo de riesgos instantáneos de Cox se puso en evidencia un cociente de riesgos instantáneos ajustados (aHR) de 10,15 (IC95% 5,67–18,17; $P < 0,05$) de TBP asociada con la NTM. La mayoría de casos de TBP (17/23 casos, 73,9%) se diagnosticó en los primeros 6 meses después del diagnóstico de NTM. Los factores de riesgo independientes de contraer TBP después de una NTM fueron la ancianidad (⩾65 años, aHR 4,45; IC95% 1,94–10,22; $P < 0,05$), el sexo masculino (aHR 1,75; IC95% 1,01–3,13; $P < 0,05$), la infección por el virus de la inmunodeficiencia humana (VIH; aHR 12,49; IC95% 3,20–48,79; $P < 0,05$) y la enfermedad pulmonar obstructiva crónica (aHR 4,46; IC95% 2,19–9,10; $P < 0,05$). La incidencia acumulada de TBP en pacientes con antecedente de NTM fue significativamente mayor que en los casos testigo ($P < 0,0001$; análisis Kaplan-Meier). Sin embargo, las tasas de supervivencia de los pacientes TBP de ambas cohortes no presentaron una diferencia significativa.

CONCLUSIÓN: El estudio permitió demostrar una mayor prevalencia de TBP después de una enfermedad causada por NTM. La infección por el VIH representó el más alto riesgo independiente de aparición posterior de TBP.