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ORIGINAL ARTICLE

Assessment of latent tuberculosis infection in psychiatric inpatients: A survey after tuberculosis outbreaks

Sheng-Wei Pan [a,b,c,d], Yu Ru Kou [d,e], Tsung-Ming Hu [f], Yen-Chih Wu [b], Yu-Chin Lee [a,c], Jia-Yih Feng [a,c], Wei-Juin Su [a,c,*]

[a] *Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan*
[b] *Department of Internal Medicine, Yuli Branch, Taipei Veterans General Hospital, Hualien, Taiwan*
[c] *School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[d] *Institute of Physiology, National Yang-Ming University, Taipei, Taiwan*
[e] *Institute of Emergency and Critical Care Medicine, National Yang-Ming University, Taipei, Taiwan*
[f] *Department of Psychiatry, Yuli Branch, Taipei Veterans General Hospital, Hualien, Taiwan*

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Abstract *Background/Purpose:* To investigate risk factors of latent tuberculosis infection (LTBI) among inpatients of chronic psychiatric wards with tuberculosis (TB) outbreaks.
Methods: In April 2013, inpatients of four all-male wards with TB outbreaks were tested for LTBI using the QuantiFERON-TB Gold in Tube (QFT) method. Based on this investigation, a retrospective study was conducted to assess risk factors for LTBI. Inpatients exposed to cluster-A or cluster-B TB cases were defined as contacts of cluster-A or cluster-B, and others, as nonclustered contacts.
Results: Among 355 inpatients with TB exposure, 134 (38%) were QFT-positive for LTBI. Univariate analysis showed that significant predictors for QFT-positivity were age, case-days of exposure to all TB cases (TB-all) and to sputum smear positive cases, number of source cases with cough, and exposure to cluster-A TB cases. Independent risk factors for LTBI were higher age [adjusted odds ratio (OR) 1.03, 95% confidence intervals (CI: 1.01–1.05)], TB-all exposure case-days $\geq$ 200 [adjusted OR 2.04 (1.06–3.92)] and exposure to cluster-A TB cases [adjusted OR 2.82 (1.30–6.12)] after adjustment for the sputum smear positivity, and cough variables of the source cases. The contacts of cluster-A had a greater risk of LTBI than did those of cluster-B, especially in the younger population ($\leq$50 years) after adjustment [adjusted OR 2.64 (1.03–6.76)].

* Corresponding author. Department of Chest Medicine, Taipei Veterans General Hospital, Number 201, Section 2, Shih-Pai Road, Taipei 11217, Taiwan.
E-mail address: wjsu@vghtpe.gov.tw (W.-J. Su).

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Conclusion: After TB outbreaks, more than one third of inpatients were QFT-positive for LTBI. Our findings suggest that, beside the infectiousness of source cases, intensity of exposure, and age of contacts, exposure to TB cases in potential genotyping clusters may be predictive for LTBI in this male psychiatric population.
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Introduction

It is estimated that one third of the world's population are infected with *Mycobacterium tuberculosis* (MTB), and that most of the infected are in a state of latent tuberculosis infection (LTBI).[1] However, a person with LTBI carries a 5—10% lifetime risk of developing active tuberculosis (TB) disease.[2—4] Residents in a long-term care (LTC) facility are at risk of TB infection because of frequent disease transmission, and they also may have comorbidities that are associated with an increased risk of TB reactivation.[3—5] In addition, people with a mental illness may have a higher risk of TB infection than the general population.[6,7] Outbreaks of active TB in psychiatric institutions are not uncommon, and LTBI among psychiatric residents may comprise a reservoir for future TB diseases.[8—10] However, the burden of LTBI in this specific population has rarely been reported.

TB infection is associated with environmental, host, and bacterial factors. Risk factors for LTBI are as follows: birth in a country with a high TB incidence, employment in a TB-related place, older age, smoking, past TB history, and frequent contact with a source case responsible for TB transmission.[11—17] Furthermore, the risk of TB infection among contacts is increased by some characteristics of the source cases, including the ability to generate cough aerosols, grading of a positive sputum smear, and presence of a cavity on radiography.[18,19] Moreover, distinct MTB strains may differ in their capacities to cause secondary TB cases and LTBI, therefore, potential bacterial factors may influence the risk of TB transmission.[20,21] TB outbreaks may result from those risk factors that contribute to LTBI. However, for residents in LTC facilities experiencing TB outbreaks, little is known about the impact of those factors on the risk for LTBI. It is particularly worthwhile to evaluate the risk factors for LTBI in LTC psychiatric inpatients because of their vulnerability to acquiring TB infection.[7] With better understanding of the risk factors for LTBI, clinicians may be able to prioritize persons with the greatest need for LTBI testing and treating.[22]

In 2012, outbreaks of TB occurred in the LTC wards of a psychiatric hospital in Taiwan, and MTB genotyping disclosed the presence of two clustered MTB strains. In addition to systemic screenings for active cases, a survey for LTBI was conducted in 2013 using a whole blood interferon-gamma release assay (IGRA).[23] Because distinct MTB strains may be associated with different degrees of infectiousness, we had a great interest in the impact of the two different clustered strains on the risk of LTBI in contacts of this facility.[21] Based on this survey, we investigated the prevalence rate and predictors of LTBI in this specific population.

Methods

Setting and participants

This was a retrospective study of inpatients in chronic psychiatric wards of Taipei Veterans General Hospital (TPEVGH), Yuli branch (Taiwan). We reviewed the medical records and LTBI reports of enrolled inpatients. This study was approved by the institutional review board (IRB number: 2014-10-005A).

The Yuli branch of TPEVGH, which has 2500 beds, provides chronic care for mentally ill patients. In this hospital, the TB incidence rate has increased markedly since 2010. Based on DNA genotypes using spoligotyping, the 15-loci mycobacterial interspersed repetitive unit variable number tandem repeat (MIRU-VNTR) method, restriction fragment length polymorphism analysis, and exposure histories, no secondary cases shared an MTB strain identical to that of the source over a 1-year period after an index case was diagnosed.[24] Despite infection control efforts, 23 consecutive cases of pulmonary TB occurred in six all-male wards from January 2012 to April 2013 (Figure 1). Among them, nine cases carried clustered MTB strains that fell into two clusters. One cluster included seven cases in Ward A1, Ward A2, and Ward A3 (cluster-A), and the other included two cases in Ward B (cluster-B). The physical environments of these wards were relatively identical. For TB control and prophylactic treatment guided by the Centers for Disease Control of Taiwan, LTBI surveys were carried out in four target wards (Ward A1, Ward A2, Ward B, and Ward C1) where two or more clustered TB cases or four or more nonclustered ones stayed during their infectious periods. Inpatients who had been admitted to the four target wards during the TB outbreak period were tested for LTBI in April 2013.

Diagnostic test for LTBI

An IGRA-based tool, the QuantiFERON-TB Gold in Tube (QFT; Cellestis Limited, Melbourne, VIC, Australia) measure, was used to diagnose LTBI in this survey. Because the decision to test is also a decision to treat,[4] the QFT test was restricted to candidates of isoniazid preventive treatment for LTBI. Hence, inpatients were excluded from LTBI screening if they: (1) refused blood testing for LTBI

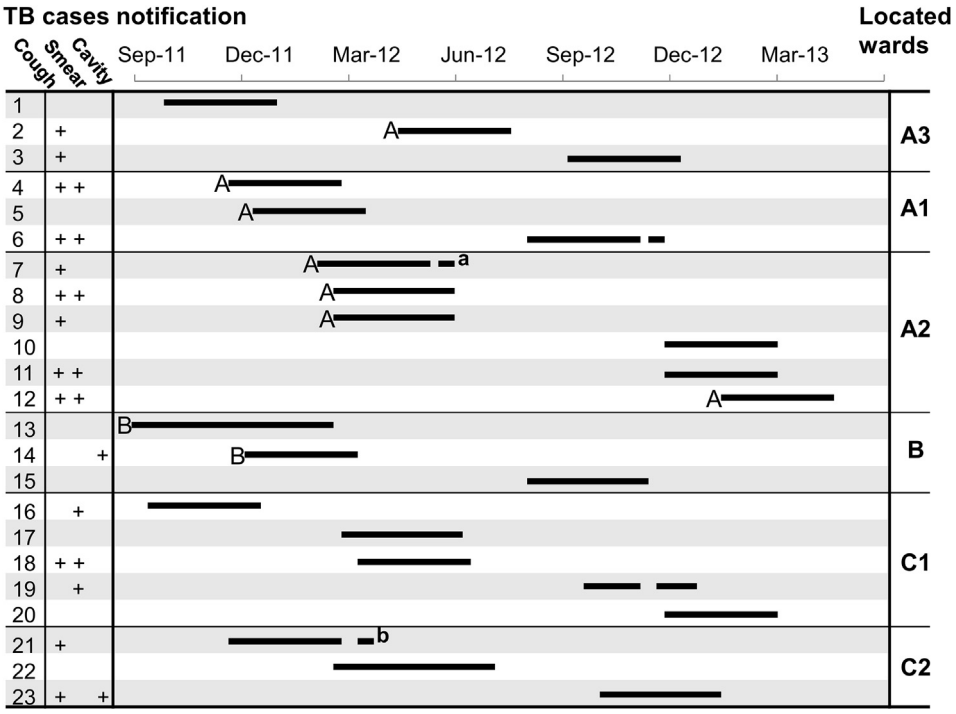

Figure 1. Characteristics of tuberculosis (TB) cases in chronic psychiatric wards during the TB outbreak period. The estimated infectious periods of the 23 TB cases, September 2011 to April 2013, are shown on the timeline. Information on the presence of cough, sputum smear positive for acid-fast bacilli, and detection of pulmonary cavities by chest roentography of each TB case is also provided. TB cases in the cluster-A or cluster-B *Mycobacterium tuberculosis* (MTB) genotyping clusters are indicated by A or B on the timeline, respectively, whereas nonclustered ones are not. The chronic psychiatric wards in which the 23 TB cases resided are also shown. [a] Had resided in Ward A1 for 9 days. [b] Had resided in Ward C1 for 4 days.

treatment; (2) had a history of complete treatment of TB before April 2013; or (3) had active TB.

The QFT test was performed as per the manufacturer's instructions. Blood was collected from selected inpatients, and interferon-gamma was released from sensitized blood lymphocytes after stimulation with MTB-specific antigens (early secretory antigenic target 6, culture filtrate protein 10, and protein TB 7.7) in a test tube. A positive response of QFT to indicate LTBI was determined if the difference in the interferon-gamma levels between the test tube (coated with antigen) and the negative control tube (nil) was $\geq$0.35 IU/mL and $\geq$25% of the nil value.[25] For this retrospective analysis, inpatients who were tested with the QFT within 8 weeks after the end of exposure were not enrolled because of the possibility of false negative results to IGRA.[25,26]

Definition and measurements

The period of TB outbreaks was defined as lasting from September 2011 to April 2013, which covered the infectious periods of the TB cases of cluster-A and cluster-B.[23] Source cases for TB transmission were defined as those testing sputum culture positive for MTB and those having had contact with any inpatient of the four target wards. The characteristics of TB cases, including the estimated periods of infectiousness, the presence or absence of coughing during their infectious periods, detection of pulmonary cavities with chest roentography, and sputum smear positive (SSP) for acid-fast bacilli, were obtained from the annual infection record in the hospital. A contact case was defined as an inpatient who lived with a TB case, within the infectious period, for >8 hours in the same ward.[27] Enrolled inpatients were classified as contacts of cluster-A or cluster-B if they had been exposed to TB cases of those clusters, even if they had also been exposed to nonclustered TB cases. Those with exposure only to nonclustered TB cases were defined as contacts of nonclustered cases.

Examining the medical charts of enrolled inpatients, we recorded the following data: age, sex, psychiatric diagnoses, comorbidities, smoking habit, limited function as bed-ridden status, findings of chest roentography, and length of stay in target wards during the outbreak periods. We also calculated the number of TB cases to whom an inpatient was exposed and the cumulative case-days of exposure. Finally, we obtained the results of QFT from LTBI report sheets. The main outcome measure was the occurrence of a positive QFT result (QFT-positive) in enrolled inpatients. The risk factors associated with the occurrence of QFT-positive were assessed.

Statistical analysis

Data are expressed as means $\pm$ standard deviation, medians with interquartile ranges (IQRs), or number (%), as appropriate. Because all of the continuous variables in this study displayed non-normal distribution, as evaluated by the Kolmogorov-Smirnov test, they are expressed as medians

with IQRs and were analyzed by Mann-Whitney *U* tests. A Chi-square test or Fisher's exact test was used to compare percentages between groups. We used univariate logistical regression analysis to identify variables associated with QFT-positive. Variables with significant differences ($p < 0.05$) on univariate analysis were included in the multivariate logistic regression. In a simplified multivariate logistic regression model, the backward elimination procedure was used to select variables to be retained in the final model. At each stage of the procedure, a variable was removed when its removal would cause a change in the exposure odds ratios (ORs) of <10%. Subsequently, a fully adjusted multivariate logistic regression analysis was constructed by including all of the important confounders. Adjusted ORs with 95% confidence intervals (95% CIs) were calculated. Statistical analysis was performed using SPSS v18.0 (SPSS Inc., Chicago, IL, USA).

Results

Characteristics of study population and prevalence rate of LTBI

The profiles of TB cases are provided in Figure 1. Among the 23 TB cases, 12 (52%) were SSP for acid-fast bacilli and eight (35%) had histories of cough. Their median duration of infectious period at wards was 94 days with an IQR of 91—103 days. Fifty (65%) of the 23 MTB isolates in TB cases belonged to the Beijing strain family, and six (26%) of them belonged to non-Beijing strains; the other two were undefined. Both of the cluster-A and cluster-B MTB isolates belonged to the Beijing strain, however, they did present with different MIRU-VNTR patterns. The flowchart of study enrollment of potential TB contacts at the four target all-male wards (Ward A1, Ward A2, Ward B, and Ward C1) is provided in Figure 2. In all, 460 inpatients were assessed using QFT tests. Because of the possibility of false negatives with QFT, 84 inpatients assessed using the QFT test within 8 weeks after TB exposure in the A2 ward were excluded from the analysis. In the end, 374 male inpatients were enrolled for LTBI analysis. Based on the definition of a contact case, 355 inpatients were TB contacts, and 144 (38%) of them were QFT-positive for LTBI. By age, the rates of LTBI among TB contacts were 26%, 25%, 48%, and 49% in the age groups of ≤35 years ($n = 35$), 36—50 years ($n = 122$), 51—65 years ($n = 145$), and >65 years ($n = 53$), respectively. By exposure, the LTBI rates were 51%, 33%, and 34% for the contacts of cluster-A ($n = 89$), of cluster-B ($n = 126$), and of nonclustered cases ($n = 140$), respectively.

Target-ward Inpatients (*N*)	Exclusion from QFT test, *N* (%)		Received QFT test, *N* (%)
	Prior TB treatment	Refusal (HBV/HCV)	
A1: 116	7 (6)	20 (17)	89 (76)
A2: 121	13 (11)	18 (15)	90 (74)
B: 188	7 (4)	19 (10)	162 (86)
C1: 167	27 (16)	21 (13)	119 (71)
Total 592	54 (9)	78 (13)	460 (78)

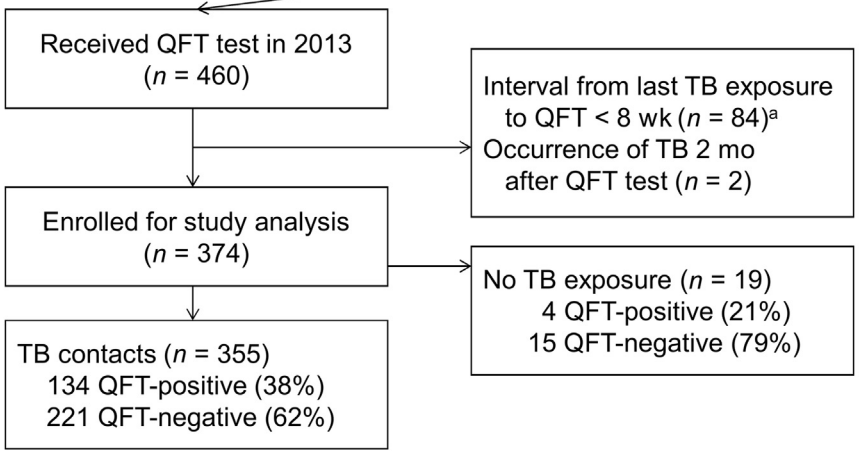

Figure 2. Study profiles presenting the number of potential tuberculosis (TB) contacts at the four target wards and the reason for exclusion. Potential TB contacts in Ward A1, Ward A2, Ward B, and Ward C1 were screened for latent TB infection. Inpatients who were not suitable for isoniazid preventive therapy were excluded from the QuantiFERON-TB Gold In-Tube (QFT) test in this hospital. The 460 inpatients were tested by QFT and were evaluated for study enrollment as shown in the flowchart. [a] All of the 84 inpatients were inmates of the target Ward A2. HBV = chronic hepatitis B; HCV = chronic hepatitis C.

Variables associated with QFT-positive LTBI among TB contacts

Table 1 shows the characteristics of the TB contacts categorized by QFT response and the results of univariate logistic regression analysis. Based on the univariate comparison of inpatients with positive and those with negative QFT responses, the significant factors associated with QFT positivity ($p < 0.05$) were older age, the number of all source cases, the cumulative case-days of exposure to all TB cases (TB-all) and SSP TB cases (TB-SSP), TB-all exposure case-days $\geq$ 200, the number of source cases with cough, and exposure to cluster-A TB cases. Those variables were considered for subsequent multivariate analysis.

Independent risk factors of QFT-positive LTBI

In the simplified multivariate model using the backward elimination method, shown in Table 2, the three significant predictors retained were age, TB-all exposure case-days $\geq$ 200, and exposure to any cluster-A TB case. In the fully adjusted multivariate logistic regression model, the independent risk factors for LTBI were higher age in years [adjusted OR 1.03, 95% CI (1.01—1.05), $p = 0.002$), TB-all exposure case-days $\geq$ 200 [adjusted OR 2.04 (1.06—3.92), $p = 0.033$], and exposure to cluster-A TB cases [adjusted OR 2.82 (1.30—6.12), $p = 0.009$] after adjustment for number of source cases, TB-SSP exposure case-days, and number of source cases with cough.

Characteristics between TB contacts of cluster-A, cluster-B, and nonclustered cases

As can be seen in Table 3, TB contacts of cluster-A had more source cases with cough and more TB-SPP exposure case-days than did the other two groups ($p < 0.05$). Compared with TB contacts of cluster-B, those of cluster-A were older and had higher numbers of source cases but fewer TB-all exposure case-days ($p < 0.05$).

Odds ratio for LTBI in groups divided by age and exposure

The rates and ORs of LTBI in the studied groups stratified by age and exposure to clustered TB cases are presented in Figure 3. For the total population, contacts of cluster-A had a twofold increased risk for LTBI compared with nonclustered contacts [adjusted OR 2.04 (1.17—3.56), $p = 0.012$] after adjustment for age and TB-all exposure case-days. Contacts of cluster-A remained at higher risk of LTBI than those of cluster-B, with a weak trend toward significance [adjusted OR 1.64 (0.90—2.99), $p = 0.109$]. For the younger group (≤50 years), contacts of cluster-A ($n = 27$) had an exponentially increased risk for LTBI compared with nonclustered contacts ($n = 58$) [adjusted OR 4.64 (1.57—13.70), $p = 0.006$]. Notably, contacts of cluster-A had a 2.6-fold higher risk of LTBI than those of cluster-B ($n = 72$), with statistical significance [adjusted OR 2.64 (1.03—6.76), $p = 0.044$]. By contrast, the risks of

Table 1 Characteristics of the tuberculosis (TB) contacts categorized by QuantiFERON-TB Gold In-Tube (QFT) response ($n = 355$) and univariate analysis of factors associated with QFT-positivity

Variables	QFT-positive ($n = 134$)	QFT-negative ($n = 221$)	Univariate analysis	
			OR (95% CI)	p[a]
Age (y)	57 (50—63)	50 (42—60)	1.03 (1.01—1.05)	<0.001
Underlying disease				
Schizophrenia	116 (87)	189 (86)	1.16 (0.61—2.17)	0.654
Organic brain syndrome	14 (11)	27 (12)	0.85 (0.43—1.67)	0.630
Mood disorder	13 (10)	17 (8)	1.30 (0.61—2.77)	0.497
Type 2 diabetes mellitus	14 (10)	26 (12)	0.88 (0.44—1.74)	0.704
Current or ex-smoker	95 (71)	167 (76)	0.79 (0.49—1.28)	0.333
Bedridden status	14 (10)	20 (9)	1.17 (0.57—2.41)	0.665
Fibrotic parenchyma lesion in CXR	15 (11)	16 (7)	1.61 (0.77—3.38)	0.204
Number of source cases	4 (3—6)	4 (3—5)	1.16 (1.00—1.34)	0.044
TB-all exposure case-days	283 (265—323)	283 (186—323)	1.00 (1.00—1.01)	0.042
TB-all exposure case-days ≥ 200	115 (86)	159 (72)	2.36 (1.34—4.16)	0.003
Number of source cases with SSP	2 (0—3)	1 (0—2)	1.17 (0.98—1.39)	0.081
TB-SSP exposure case-days	133 (0—167)	68 (0—167)	1.00 (1.00—1.01)	0.019
Number of source cases with cough	3 (0—3)	1 (0—3)	1.17 (1.01—1.36)	0.038
Exposure to TB cases with cavity	42 (31)	80 (36)	0.81 (0.51—1.27)	0.351
Exposure to any cluster-A TB case	45 (34)	44 (20)	2.03 (1.25—3.31)	0.004
Exposure to any cluster-B TB case	42 (31)	84 (38)	0.75 (0.47—1.17)	0.204
Exposure only to nonclustered TB case	47 (35)	93 (42)	0.74 (0.48—1.16)	0.191

[a] Using univariate logistic regression analysis of factors associated with QFT-positivity.
All continuous data are expressed as median (interquartile range) due to their non-normal distribution and categorical data are expressed as number (%).
CI = confidence interval; CXR = chest X-ray; QFT = QuantiFERON-TB Gold in Tube test; OR = odds ratio; SSP = sputum smear positivity; TB = tuberculosis.

Table 2 Multivariate logistical regression analysis for potential risk factors of latent tuberculosis (TB) infection diagnosed by QuantiFERON-TB Gold in Tube test (QFT)

Variables	Simplified model using backward elimination method		Fully adjusted model adding important confounders	
	aOR (95% CI)	*p*	aOR (95% CI)	*p*
Age (y)	1.03 (1.01–1.04)	0.003	1.03 (1.01–1.05)	0.002
Number of source cases	–[a]		1.13 (0.87–1.47)	0.364
TB-all exposure case-days	–[a]		–[b]	
TB-all exposure case-days ≥ 200	1.90 (1.06–3.40)	0.032	2.04 (1.06–3.92)	0.033
TB-SSP exposure case-days	–[a]		0.99 (0.99–1.00)	0.096
Number of source case with cough	–[a]		1.07 (0.82–1.40)	0.625
Exposure to any cluster-A TB case	1.75 (1.06–2.89)	0.030	2.82 (1.30–6.12)	0.009

[a] Entered into multivariate logistic regression analysis using backward elimination method but not retained in the final model.
[b] The continuous variable, TB-all exposure case-days, is highly correlated with its dichotomous variable, TB-all exposure case-days > 200 (Pearson correlation coefficient 0.866, $p < 0.001$); thus, they must be excluded from each other before entry in the fully adjusted model. In addition, TB-all exposure case-days is an inferior marker to TB-all exposure case-days > 200 because the former was removed in the backward elimination procedure. Hence, the dichotomous variable was entered in the fully adjusted model instead of TB-all exposure case-days.
aOR = adjusted odds ratio; CI = confidence interval; SSP = sputum smear positivity.

LTBI were not statistically different between the subgroups for the older group (>50 years).

Discussion

We found a high prevalence rate of LTBI (38%) among LTC psychiatric inpatients of all-male wards after outbreaks of TB. After adjustment for the SSP and cough variables of source cases, we also identified three independent risk factors for LTBI among contacts: older age, case-days of exposure ≥200, and exposure to cluster-A TB cases. Moreover, our study showed that contacts of cluster-A had a 2.6-fold increase in the risk for LTBI compared with those of cluster-B in the younger population. Thus, we discovered that exposure to TB cases carrying clustered strains of different genotypes may be associated with diverse risks for LTBI among this population.

The prevalence rate of LTBI in our study was within the range of 17–88% previously reported in residents of LTC facilities worldwide.[9,12,28,29] However, for a TB-endemic area with an intermediate TB burden, our LTBI rate of 38% is relatively higher than the 26.6% found in another mixed high-risk population in Taiwan.[30,31] Of note is that our rate was double that of household TB contacts; one study reported a 19% rate of QFT-positivity in Taiwan.[32] The higher mean age and greater exposure to source cases in our population may have contributed to the difference. Interestingly, even in a selected subgroup with an age of ≤35 years old, our psychiatric inpatients had a nearly twofold higher rate of LTBI than that found in another study in a Taiwan prison (age < 35 years, 14% QFT-positivity).[33] To this end, this difference may be explained by the existence of TB outbreaks and some unique characteristics of our population, including mental illness with vulnerability to infection.[6] Actually, because of the alarming LTBI rate of

Table 3 Characteristics of the tuberculosis (TB) contacts categorized by source-case clusters ($n = 355$)

Variables	Contacts of cluster-A ($n = 89$)	Contacts of cluster-B ($n = 126$)	Contacts of noncluster ($n = 140$)
QFT-positive for LTBI	45 (51)	42 (33)*	47 (34)*
Age (y)	58 (48–65)	49 (40–54)*	56 (45–65)
Number of cluster-A source case	3 (3–3)	0*	0*
Number of cluster-B source cases	0	2 (2–2)*	0
Number of nonclustered source cases	1 (1–1)	1 (1–1)	6 (2–6)*
Number of source cases	4 (4–4)	3 (3–3)*	6 (2–6)*
Number of source cases with SSP	2 (2–2)	0*	3 (1–3)*
Number of source cases with cough	3 (3–3)	0*	3 (1–3)*
TB-all exposure case-days	283 (260–283)	318 (246–323)*	316 (136–363)
TB-all exposure case-days ≥ 200	76 (85)	103 (82)	95 (68)*
TB-SSP exposure case-days	191 (161–191)	0*	138 (50–167)*

Continuous data expressed as median (interquartile range) and categorical data as number (%).
* Indicates a significant difference ($p < 0.05$) between contacts of cluster-A TB cases and compared groups.
LTBI = latent tuberculosis infection; QFT = QuantiFERON-TB Gold in Tube test; SSP = sputum-smear positivity.

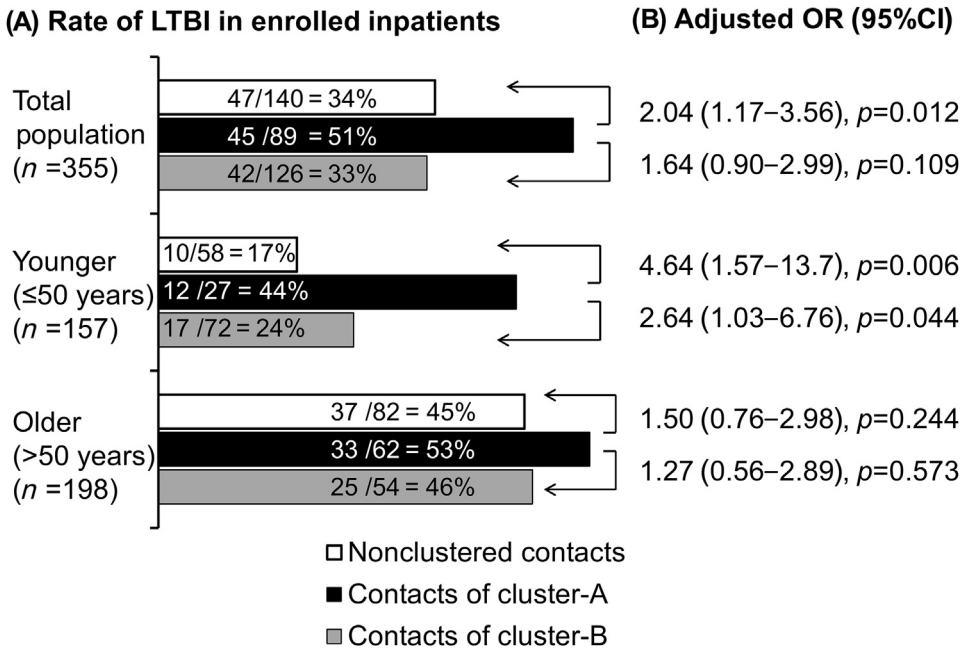

Figure 3. Rate and risk of latent tuberculosis (TB) infection (LTBI) in subgroups stratified by age and exposure to clustered TB cases. In the total population, the numbers of QuantiFERON-TB Gold In-Tube (QFT)-positive (*n*) and QFT-tested (*N*) cases and rates of LTBI (*n*/*N*) among contacts of nonclustered, cluster-A, and cluster-B TB cases are shown. These data in younger (≤50 years) and older groups are also provided, respectively (A). The risk of LTBI among contacts of cluster-A TB cases is compared to the other two contact groups in the total population and in the younger and older groups correspondingly. (B) Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) are provided. Adjusted factors were age and cumulative case-days of exposure to all TB cases.

38%, the supervisor of this hospital implemented active TB screening for all LTC residents annually and prophylactic treatment of targeted inpatients after the survey.

In contrast to prior cross-sectional studies, we evaluated predictors for LTBI among psychiatric inpatients, targeting both hosts and bacterial factors. Not surprisingly, older age and more case-days of exposure were found to be significant predictors for LTBI in this study. Our novel finding is that exposure to TB cases carrying the cluster-A MTB strain is independently predictive of LTBI after adjustment for cofactors including the source case's SSP and cough variable. To our knowledge, this is the first study, on the basis of genotyping of MTB isolates, to identify exposure to TB cases carrying potential genotypes as an independent risk factor for LTBI among LTC psychiatric inpatients.

Recently, a study of household contacts proposed that distinct MTB strains may be associated with diverging infectiousness, which is indicated by contacts' responses to the tuberculin skin test.[21] However, another population-based study did not find a strain difference in TB transmission according to the rate of secondary TB cases.[34] In our study, the two groups of psychiatric inpatients who contacted cases carrying two distinct MTB genotypes presented diverse risks for QFT-positive LTBI after adjustment for confounding factors. Furthermore, the risk diversity between the two groups increased in the younger population but diminished in the older one. We thought that the younger population might have a lower rate of pre-existing remote LTBI, which could unmask this strain-associated risk diversity.[29] By contrast, in the older groups, the risk difference between contacts of cluster-A and cluster-B may have been diluted by a higher burden of remote LTBI and thus become less evident. Our findings suggest that cases carrying different MTB strains may incur distinct risks of TB infection among contacts. However, additional studies will be needed to explore potential MTB genotypes and adjust for other confounding host factors to determine strain-specific infectivity.

Our study had several limitations. First, all of the participants were inpatients in all-male wards, and 78 (13%) inpatients with hepatitis B or hepatitis C refused the LTBI survey. Whether our findings can be generalized to a female population or those with hepatitis B or hepatitis C is uncertain. Second, the inpatients' proximity to the TB cases could not be fully evaluated because the study was retrospective. Nevertheless, on the basis of inpatients' sharing a space with TB cases, we calculated the exposure case-days to assess their intensity of exposure to source cases with SSP or in total.[27] However, it is still difficult for risk adjustment to fully account for other factors, such as cough duration of TB cases, population density, and group activity of inpatients. Third, no nonpsychiatric or nonhospitalized control group in the same facility was available for analysis to clarify the association between LTBI and psychiatric inpatients. In addition, no data on the prevalence rate of LTBI before TB outbreaks in this population were available for comparison. Finally, we could not clarify recently acquired LTBI because of the absence of baseline QFT data before TB exposure.

In conclusion, after TB outbreaks, more than one-third of the exposed psychiatric inpatients in the LTC all-male wards were QFT-positive for LTBI. With such a high burden

of both active and latent TB, all inpatients of this hospital should be considered at high risk for TB infection. For this specific population, older age, case-days of exposure ≥200, and exposure to cluster-A TB cases were independent risk factors for LTBI after adjustment for cofactors. Our findings also suggest that exposure to TB cases of different genotyping clusters may be associated with diverse risks for LTBI. Further studies will be needed to investigate the association between exposure to potential MTB genotypes and the risk of LTBI among contacts.

Conflicts of interest

All contributing authors declare no conflicts of interest.

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