Risk factors associated with TB, a case-control study in a Chinese population

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Background: Tuberculosis (TB) remains one of the leading communicable diseases in the world, and this case-control study was conducted to explore potential risk factors for TB.

Methods: A total of 104 new TB patients were collected in 2011, and each 2 cases were matched with one healthy control. A standardized questionnaire was applied for risk factors collection. Multivariate logistic regression analysis was employed for multi-factors analysis, and the association between related factors and TB risk were estimated by odds ratio (OR) and 95% confidence intervals (95% CI).

Results: Multivariate logistic regression showed that frequent fruits intake and physical activity, high body mass index (BMI) were associated with decreased risk of TB (OR =0.20, 95% CI: 0.08–0.53; OR =0.41, 95% CI: 0.17–1.00; OR =0.86, 95%CI: 0.76–0.97; respectively), while diabetes mellitus (DM) and no ventilation of working place were related to increased risk of TB (OR =12.99, 95% CI: 1.30–129.58; OR =3.39, 95% CI: 1.24–9.26; respectively).

Conclusions: Lower BMI might be susceptible to TB, and frequent fruits consumption and more physical activity would low the risk of TB. Meanwhile, ventilation of working place and DM treatment will be in the necessity for TB control.

Keywords: Tuberculosis (TB); risk factors; diabetes; body mass index (BMI); case-control

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Introduction

It was estimated 10.4 million new tuberculosis (TB) cases worldwide in 2015, and 34% among women and 10% among children. Meanwhile, over 10% TB cases were co-infected with human immunodeficiency virus (HIV). Moreover, there were 1.4 million TB deaths in 2015 and 0.4 million deaths were resulted from HIV co-infection (1). China now accounts for 10% of the total new TB cases, and ranks the third place of TB case burden. Clinical symptoms, such as coughing, expectoration or emptysis lasting for more than two weeks, were strong indications of TB (2). However, those symptoms only occurred when the adult was much likely to be involved in TB disease.

Identifying risk factors on TB before the disease occurrence is important for TB control. Recent studies have revealed that smoking status would be associated with increased risk of TB infection and the reduced TB treatment success rate (3,4), and smoking cessation was important during TB treatment (5,6). Changes in lifestyle and diet have been contributing to an increased prevalence of diabetes mellitus (DM) in many low-income and middle-income countries where TB control is in a severe situation as well, and the risk of TB was increased among persons with DM (7). Thus, screening out TB associated risk factors

will be a benefit in TB control prior to the occurring of TB. In this study, a retrospective case-control study was conducted to explore potential risk factors which might be correlating with TB susceptibility in a Chinese population.

Methods

A total of 104 new incident pulmonary TB were enrolled in this study in 2011, all of the patients were smear positive and with no previous TB disease history. Meanwhile, every two TB cases in the same region were matched with one healthy control from the same area by age (±5 years), gender. All the enrolled participants were collected from the outpatient of the municipal center for diseases control and prevention of Jiangsu province. Finally, 52 healthy participants were selected as the control group, and all the controls were examined with no TB symptoms and demonstrated no signs of TB by X-ray. The study was approved by the ethics committee of Jiangsu Provincial Center for Disease Control and Prevention.

A standardized designed questionnaire containing the last year's living conditions and habits were adopted for this case-control study. The living conditions and habits were mainly as follows: (I) ventilation of working place; (II) the frequency of physical activities, classified as (i) no less than once a week, (ii) no less than once a month and less than once a week, (iii) less than once a month; (III) smoking and drinking status, one cigarette per day for over one year was considered as smoking and three or more alcohol drinks a week for over 6 months was defined as drinking; (IV) frequency of fruits and meat consumption, the frequency was classified as (i) no less than once a week, (ii) no less than once a month and less than once a week, (iii) less than once a month; (V) going to clustering site, such as net bar, cinema, etc.; (VI) TB patient contacting history; etc.

Statistical analysis

The between-group demographics were compared by unpaired Student t test or χ^2 test. Multivariate logistic regression analysis was employed for multi-factors analysis, and the association between related factors and TB risk were estimated by computing the odds ratio (OR) and 95% confidence intervals (95% CI). Statistical significance level was considered as <0.05. All statistical analyses were conducted by SAS software (V9.1.3, SAS Institute, Inc., Cary, NC, USA).

Results

The basic characteristics of TB cases and the healthy controls were described in *Table 1*. Fifty-two healthy controls were matched to TB cases on age and gender (P=0.9703 and 0.5551, respectively). Education and occupation of TB cases and controls showed no statistically significant difference (P=0.0846 and 0.1475, respectively). Also, the frequency of meat consumption in TB case and the controls showed no statistically significant difference (P=0.5488). However, the proportion of fruits consumption was different among TB cases and the controls (P=0.0052), the percentages of fruits consumption for no less than once a week in the controls (76.9%) was higher than TB cases (50.0%). Smoking and drinking habits among TB cases and control showed no variance. It was found the frequency of physical activities in TB cases were significantly lower than that of the controls (P=0.0243). Specifically, the proportion of subjects in TB cases (68.3%) with physical activities less than once a month was quite higher than those of the controls (48.1%). For living conditions, short of ventilation for working place would be another risk factors for TB, our data showed that 51.9% of healthy controls reported ventilation facilities being equipped within the working place, which was much higher than TB cases (35.6%, P=0.0203). Contacting history of TB patients also showed a statistically significant difference among TB cases (32.7%) and the controls (23.1%) (P=0.0232). The body mass index (BMI) was 23.01±3.05 in the healthy controls, which was significantly higher than that of TB cases (21.19±3.91, P=0.0038). In this study, the proportion of the medical insurance for TB cases (72.1%) was quite lower than controls (94.2%, P=0.0013).

Then, those factors individually related to TB risk were put together in the multi-factors analysis by multivariate logistic regression (*Table 2*). Age (continuous data: year), gender (category: 0 = male, 1 = female), occupation (category: 0 = peasant, 1 = non-peasant), fruits (0 = less than once a week, 1 = no less than once a week), smoking (category: 0 = no, 1 = yes), drinking (category: 0 = no, 1 = yes), physical activities, (category: 0 = less than once a week, 1 = no less than once a week), DM (category: 0 = no, 1 = yes), TB patients contacting history 1 (category: 0 = no, 1 = yes), TB patients contacting history 2 (category: 0 = no, 1 = unclear), ventilation of working place (category: 0 = yes, 1 = no), BMI (continuous data: kg/m^2) were included in the model. It was found that fruits consumption for no less than once a week might associate with a decrease risk of

Table 1 Basic characteristics of pulmonary tuberculosis cases and healthy controls

Variables	Cases (n=104) (%)	Controls (n=52) (%)	P value
Age (year)	48.09±17.34	48.19±16.26	0.9703[a]
Gender			0.5551
Male	65 (62.5)	35 (67.3)	
Female	39 (37.5)	17 (32.7)	
Education			0.0846
Primary school and lower	15 (14.4)	3 (5.8)	
Middle school and lower	52 (50.0)	22 (42.3)	
High school and above	37 (35.6)	27 (51.9)	
Occupation			0.1475
Peasant	38 (36.5)	13 (25.0)	
Non-peasant	66 (63.5)	39 (75.0)	
Meat-consumption			0.5488
No less than 1/week	92 (88.5)	48 (92.3)	
No less than 1/month and less than 1/week	10 (9.6)	4 (7.7)	
Less than 1/month	2 (1.9)	0 (0.0)	
Fruits			0.0052
No less than 1/week	52 (50.0)	40 (76.9)	
No less than 1/month and less than 1/week	18 (17.3)	5 (9.6)	
Less than 1/month	34 (32.7)	7 (13.5)	
Physical activities			0.0234
No less than 1/week	29 (27.9)	26 (50.0)	
No less than 1/month and less than 1/week	4 (3.8)	1 (1.9)	
Less than 1/month	71 (68.3)	25 (48.1)	
Smoking			0.9086
No	61 (58.7)	30 (57.7)	
Yes	43 (41.3)	22 (42.3)	
Drinking			0.2128
No	57 (54.8)	23 (44.2)	
Yes	47 (45.2)	29 (55.8)	
Medical insurance			0.0013
No	29 (27.9)	3 (5.8)	
Yes	75 (72.1)	49 (94.2)	
Diabetes status			0.0559
No	93 (89.4)	51 (98.1)	
Yes	11 (10.6)	1 (1.9)	

Table 1 *(continued)*

Table 1 *(continued)*

Variables	Cases (n=104) (%)	Controls (n=52) (%)	P value
Clustering sites			0.3644
No	52 (50.0)	22 (42.3)	
Yes	52 (50.0)	30 (57.7)	
Ventilation of working place			0.0203
Yes	37 (35.6)	27 (51.9)	
No	67 (64.4)	25 (48.1)	
TB patients contacting history			0.0232
Yes	24 (23.1)	17 (32.7)	
No	53 (51.0)	31 (59.6)	
Not clear	27 (26.0)	4 (7.7)	
BMI (kg/m^2)	21.19±3.91	23.01±3.05	0.0038[a]
Sleep hours (hours)	8.06±1.48	7.79±1.53	0.3332[a]

[a], Student unpaired *t* test. TB, tuberculosis; BMI, body mass index.

Table 2 Multivariate logistic regression analysis of risk factors in relationship with PTB

Variable	β	OR (95% CI)	*CHISQ*	P value
Age (year)	–0.028	0.97 (0.94–1.00)	3.2177	0.0728
Gender (0 = male,1 = female)	0.0763	1.08 (0.34–3.47)	0.0164	0.8981
Occupation (0 = peasant, 1 = non-peasant)	0.2451	1.28 (0.42–3.91)	0.1848	0.6672
Fruits (0 = less than once a week, 1 = no less than once a week)	–1.617	0.20 (0.08–0.53)	10.476	0.0012
Smoking (0 = no, 1 = yes)	–0.275	0.76 (0.25–2.28)	0.2404	0.6239
Drinking (0 = no, 1 = yes)	–0.127	0.88 (0.33–2.33)	0.0658	0.7976
Physical activities (0 = less than once a week, 1 = no less than once a week)	–0.883	0.41 (0.17–1.00)	3.8682	0.0492
Diabetes status (0 = no, 1 = yes)	2.5642	12.99 (1.30–129.58)	4.7742	0.0289
TB patients contacting history 1 (0 = no, 1 = yes)	–0.33	0.72 (0.29–1.77)	0.517	0.4721
TB patients contacting history 2 (0 = no, 1 = unclear)	1.5146	4.55 (1.13–18.30)	4.5464	0.0330
Ventilation of working place (0 = yes, 1 = no)	1.222	3.39 (1.24–9.26)	5.692	0.0170
BMI (kg/m^2)	–0.152	0.86 (0.76–0.97)	6.2846	0.0122

PTB, Pulmonary tuberculosis; TB, tuberculosis; BMI, body mass index.

TB (OR =0.2, 95% CI: 0.08–0.53, P=0.0012). Participants with physical activities no less than once a month may also associate with a reduced risk of TB (OR =0.41, 95% CI: 0.17–1.00, P=0.0492). However, DM may relate to an increased risk of TB (OR =12.99, 95% CI: 1.30–129.58, P=0.0289). Meanwhile, no ventilation facilities in the working place may associate with an increased risk of TB (OR =3.39, 95% CI: 1.24–9.26, P=0.0170), and those participants with higher BMI may associate with a decreased risk of TB (OR =0.86, 95% CI: 0.76–0.97, P=0.0122). However, the multivariate logistic regression demonstrated that contacting history of TB did not reach statistical significance in relation to the risk of TB.

Discussion

Today, nearly 1/3 of the world population was infected with *Mycobacterium* TB, and around 10% of them will subsequently suffer TB. Studies have revealed that people would be more susceptible to TB when in the low immunity status, and people with immunity problems, such as with the low level of CD4+ cell counts, were more likely to be involved in TB. Except the host immune factors that would possibly increase the risk of TB, this case-control study will explore potential risk factors, mainly on living conditions and habits, which might be equally crucial in the increased risk of TB. It was found that the physical activity, fruits consumption and the higher BMI would decrease the risk of TB. On the contrary, DM and scarce ventilation of working place were the risk factors for TB.

The inverse relationship between BMI and TB mortality was revealed by Shor-Posner *et al.* (8). Recently, a larger cohort study conducted in Hong Kong elderly health-center patients found that obese and overweight BMI decreased the risk of TB when compared to normal or underweight BMI patients (9). For people entangled with immunity problems, Shuter *et al.* showed that overweight individuals had slower disease progression and lower viral load among AIDS-free HIV positive subjects in New York City, after adjusting for baseline CD4+ cell count and time to antiretroviral initiation (10). Meanwhile, Hanrahan et al, conducted a prospective cohort study on BMI and TB incidence and mortality in AIDS-free HIV positive adults, and they found that when compared to normal BMI subjects, adults with overweight and obese BMI were at a significantly reduced risk of TB and TB mortality (11). In this study, although BMI in both groups was in normal range according to WHO classification (12), TB patients had a significantly lower BMI than that of healthy controls, which was consistent with the previous findings. Then, once the participants with DM in the cases and the controls excluded from the analysis, and it was found that BMI of the control group was also significantly higher than that of the cases (data was not shown).

In 2010, WHO estimated that 285 million people were living with DM, of whom 7 million people developed the disease during that year and 3.0 million deaths were attributed to DM, and current predictions estimate that the prevalence of DM will reach 438 million by 2030 and that 80% of prevalent cases will occur in developing countries (13). Meanwhile, China and India took the first two places holding the utmost DM cases. The increase in the number of people with DM may further complicate the care and the control of TB, especially in many areas with a high burden of the both diseases (14,15). Among those with active TB, DM may adversely affect TB treatment outcomes by delaying the time to microbiological response, reducing the likelihood of a favorable outcome, and increasing the risk of relapse or death (16). A study conducted by Stevenson *et al.* demonstrated that DM accounted for 80% of incident pulmonary TB among people with DM, and 14.8% of incident TB in the total population in India (17). In this case-control study, it was found DM significantly associated with the risk of TB.

Ventilation was necessary for controlling TB transmission (18). This study provided the evidence that adequate ventilation of the working place would significantly decrease the risk of TB. Ventilation of the working place was not only important for the general, but especially crucial for those working in the nosocomial areas. One study in South India showed that the latent TB infection (LTBI) was nearly 50% of the young nurse trainees (19), which indicated a serious situation of nosocomial transmission of TB, and the optimized ventilation facilities are in necessity for clinics and wards, and even prophylactic medicine would be necessary for the health workers.

People with contacting history of TB will be at high risk of infection, especially for those under household contacts history (18,20,21). Recently, interferon-gamma release assays (IGRAs) and tuberculin skin testing (TST) were applied for detecting LTBI of family members of TB patients, and those two methods will give a good suggestion for LTBI and chemoprophylaxis of TB (22,23). In this study, 26.0% of TB cases were not sure whether they had contacted with TB patients, while only 7.7% of the controls were not certain about TB contacting. Thus, the association

between TB contacting history and risk of TB will not be reached in this study.

The limitations of this study should be mentioned. Retrospective bias could not be avoided in case-control studies, especially for those with uncertain answers, which may induce plausible results. Also, other potential risk factors on TB cannot be discussed due to the limited sample size.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jphe.2017.05.09). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the ethics committee of Jiangsu Provincial Center for Disease Control and Prevention. Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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