

Letter to the Editor

**Risk of Active Pulmonary Tuberculosis among Patients with Coal Workers' Pneumoconiosis: A Case-control Study in China***

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The aim of this study was to estimate the association between occupational, environmental, behavioral risk factors, and active pulmonary tuberculosis (PTB) among coal workers' pneumoconiosis (CWP) patients. A matched case-control study was conducted in 86 CWP patients with active PTB and 86 CWP controls without TB. A standardized questionnaire was used for risk factors assessment. Conditioned logistic regression analysis was used to identify associations between the risk factors and active PTB among CWP patients. The results showed that the stage of CWP, poor workplace ventilation, family history of TB, and exposure to TB were independent risk factors for active PTB in patients with CWP with which recommendations for improving work environments, and for case finding activities in patients with CWP could be made.

Key words: Pulmonary tuberculosis; Coal workers' pneumoconiosis; Risk; Case-control study

Pneumoconiosis is a well-known occupational fibrotic lung disease with no specific treatment currently available. China has one of the highest rates of pneumoconiosis in the world. It accounts for over 85% of all reported occupational diseases in the country. Coal workers' pneumoconiosis (CWP) is believed to be the commonest type, accounting for approximately 60% of the total number of new cases of pneumoconiosis^[1]. The association between pneumoconiosis and pulmonary tuberculosis (PTB) has been well established in previous studies. Epidemiological studies and case reports have verified that workers exposed to silica dust have increased morbidity and mortality from PTB^[2].

Therefore, the prevention and control of the risk of contracting PTB in patients with CWP, thereby preventing *M. tuberculosis* infection and the development of PTB, is crucial. To further evaluate the occupational, environmental, and behavioral risk factors influencing the development of PTB in patients with CWP, we performed a matched case-control study.

The present matched case-control study was conducted at the Hunan Institute for Tuberculosis Control (HITC) and the Hunan Prevention and Treatment Center for Occupational Diseases (HPTCOD), between April and November, 2017. HITC, an 800-bed specialized TB hospital, and HPTCOD, a 520-bed specialized occupational diseases hospital, are located at Changsha, Hunan Province, China. HITC has more than 1,000 TB hospitalizations and HPTCOD has 2,000 occupational disease hospitalizations each year. The study protocol was approved by the Ethical Clearance Committee of the National Institute of Occupational Health and Poison Control of the Chinese Center for Disease Control and Prevention. All study participants provided written consent.

A sample size of 86 case-control pairs was estimated to be sufficient to detect a significant association between active TB and risk factors among CWP patients. Cases were CWP patients with active PTB (CWP-TB) diagnosed using the 'WS 288-2017'^[3] diagnostic criteria for PTB, while controls were CWP patients without TB (CWP only), reconfirmed based on the 'GBZ 70-2015'^[4] diagnostic criteria for pneumoconiosis using a good quality chest X-ray. For each case, non-TB CWP patients,

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matched in ethnicity, sex and age group, were selected as controls. Cases were recruited from all wards within HITC and controls were selected from HPTCOD. The selection of controls was started after completion of the selection of cases to allow for age, sex, and ethnicity differences (Table S1 available in the www.besjournal.com).

Information on a wide range of host characteristics, and occupational, environmental, and behavioral factors relevant to active TB was collected from the cases and controls. The host information collected included body mass index (BMI), highest educational level, marital status, family size, and place of residence. Occupational factors included the stage of CWP, years of work, dust exposure period, age at which exposure to dust was initiated, and length of dust exposed employment. Environmental and behavioral factors obtained included workplace ventilation, accommodation, smoking, and alcohol consumption, among others.

BMI was calculated as the ratio between body weight in kilograms and squared body height in meters (kg/m^2). Stages of CWP were confirmed based on the 'GBZ 70-2015' diagnostic criteria for pneumoconiosis by performing a good quality chest X-ray. Smoking index was defined as the product of the number of cigarettes smoked per day and years of smoking. Smoking frequently was defined as a person who smoked more than one cigarette per day for more than 6 months, whereas, smoking occasionally was defined as a person who smoked cigarettes more than four times every week but less than once per day. Drinking frequently was defined as a person who consumed alcohol more than one day a week, whereas occasional drinking was defined as a person who consumed alcohol less than one day a week. Frequent intake of fruit was defined as a person who ate fruit no less than two days a week, occasional intake of fruit as a person who ate fruit less than two days a week but no less than one day a month, and never eating fruit as a person who ate fruit less than one day a month. Doing physical exercise frequently was defined as a person who exercised for 30 or more minutes no less than three days a week, doing occasional physical exercise as a person who exercised for 30 or more minutes less than three days a week but no less than one day a month, and never doing physical exercise as a person exercised for 30 or more minutes less than one day a month. Each study participant was interviewed in person with a standardized questionnaire.

The questionnaire data was entered into the Epi Data v3.1 program (Epi Data Association, Odense, Denmark) and was analyzed using Epi-Info version 7.2.2.2 (CDC, Atlanta, GA, USA). Analysis was done using the index case and control pairs to assess the effect of risk factors. Odds ratios (*ORs*) and their 95% confidence intervals (*CI*s) were estimated using conditional logistic regression, with active TB as the outcome. Univariable analyses were performed to examine the effect of each variable of interest on the risk of active TB. A multivariable model was then constructed, including variables that showed a significant statistical effect by univariable analyses ($P < 0.05$). Finally, a combined host, occupational, environmental, and behavioral multivariable model was constructed. The adjusted *ORs* and their 95% *CI*s were calculated.

For the study, 86 cases (CWP-TB) and matched controls (CWP only) were recruited from the HITC and HPTCOD. They were all males of Han ethnicity. Of the 86 cases, 44 (51.2%) were diagnosed by clinical examination, chest radiographs, and their responses to treatment, whereas 42 (48.9%) showed a positive smear or culture for PTB. The mean age in the CWP-TB and CWP only groups was 57.3 ± 8.9 , and 56.2 ± 9.2 years, respectively, while the mean BMI was 21.7 ± 2.6 , and 22.4 ± 3.0 , respectively. There was no significant difference between the CWP-TB and CWP only groups in terms of age ($P = 0.410$), BMI ($P = 0.076$), highest education level ($P = 0.635$), and marital status ($P = 0.755$), implying no significant association. Only one participant had been vaccinated with the bacillus Calmette-Guerin (BCG) vaccine, therefore this study did not analyze its protective effect. Furthermore, all participants tested negative for HIV.

Table 1 shows the assessment of host characteristics, occupational, environmental, and behavioral risk factors for active PTB disease among CWP patients. Using univariate analysis, the occupational risk factors identified for active PTB were the stage of CWP, the age at which exposure to dust was initiated, and the length of dust exposed employment. Using the subgroup stage I CWP as a comparison, the *OR* was elevated for stage II (*OR*: 8.19; 95% *CI*: 2.36-28.38), and stage III (*OR*: 2.21; 95% *CI*: 0.69-7.10). Using the subgroup age at first dust exposure (< 18 years) as a comparison, the *OR* was elevated for the 18-29 years age group (*OR*: 1.91; 95% *CI*: 0.71-5.13), and the ≥ 30 years age group (*OR*: 3.99; 95% *CI*: 1.25-12.80). There was no significant association with the dust exposure period. The

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