

Tuberculosis prevalence among university freshmen in Zhengzhou, China, during 2004-2013

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Abstract

Background: Tuberculosis (TB) is a major public health concern worldwide, and spreads more easily in densely populated areas such as school campuses.

Objectives: The aim of this study was to determine the prevalence of positive TB skin tests among freshmen, i.e. newly-enrolled college students, in Zhengzhou City, China.

Methods: We reviewed the data of purified protein derivative (PPD) skin tests in 656,212 freshmen in 2004-2013.

Results: A positive test showed a diameter of swelling ≥ 5 mm. The PPD positive rate was 40.69 %, with a prevalence of 146.29 per 100,000. During the 10-year study period, the rate of students with positive PPD test increased from 34.19 % in 2004 to 40.69 % in 2013. The positive PPD rate was significantly higher in males than in females (41.68 % vs 39.61 %, $P < 0.0001$), and in rural compared with urban areas (42.04 % vs 38.03 %, $P < 0.0001$).

Conclusion: These findings indicated a high prevalence of PPD positivity among participants during the study period, with an increasing trend. Therefore, this population needs to be targeted by TB prevention and control programs.

Keywords: Tuberculosis; PPD test; freshmen; positive rate; prevalence.

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Introduction

Where there are humans, *Mycobacterium tuberculosis* (MTB) seems to be present as well. Tuberculosis (TB) has been a powerful deterrent to worldwide health since ancient times, and the main cause of death due to bacterial infection¹. Currently, TB is the seventh most common disease worldwide, a trend projected to continue until 2020². According to yearly WHO global TB reports since 1997²⁻⁸, statistical results from 1990 to 2015 showed that TB related deaths declined from 2 to 1.4 million, but new cases are on the rise, from 8.47 to 10.4 million. TB remained one of the top 10 causes of death worldwide in 2015⁸. Indeed, over the past decade, reports on the tuberculosis epidemic have originated from many African and Asian

countries such as Vietnam, Philippines, Ethiopia, Korea, Japan, China, India, et al.⁹⁻²⁰

However, not enough precise data are available to determine whether the back-and-forth trend will re-emerge. Worldwide, TB incidence has declined by only 1.5 % from 2014 to 2015.²¹ This needs to increase to a 4–5 % annual decline by 2020 to reach the first milestone of the End TB Strategy⁸. TB was a leading cause of adult mortality in low- and middle-income countries, ranking third after HIV and ischemic heart disease among individuals aged 15–59 years in 2001²². Besides the suffering caused by TB in humans, the monetary burden was estimated to have exceeded US\$ 56 billion, up from US\$ 3.5 billion in 2006 to US\$ 6.7 billion in 2015. This is in part due to the WHO Millennium Development Goals (MDG) and Stop TB Partnership targets for 2015, which aim to halt and reverse TB incidence, halve prevalence and mortality rates compared to 1990 levels, detect at least 70% of infectious cases, and successfully treat 85% of the infectious cases detected²³. The more important long-term elimination target set for 2050 will not be met with current strategies and tools. Global actions and investments fall far short of those needed to end the global TB epidemic⁸. Several key challenges persist, including unaffordable sufficient quality services to vulnerable people, multidrug-resistant *M. tuberculosis* strains, underlying social determinants in the community, and obsolete and inadequate technologies for diagnosis, treatment, and prevention²⁴. China had the second largest number of new TB cases after India in 2004–2013^{7,25}. The Fifth National Tuberculosis Epidemiological Survey (FNTES) in 2010 showed declined TB prevalence in China²⁶. However, specific groups appear to be at higher risks, including freshmen from TB epidemic backgrounds, underdeveloped regions, and even some unexpected places such as college and university campuses. This high incidence could lead to widespread outbreaks if ignored. The objective of the present study was to appraise the TB epidemic in colleges and universities, exploring effective measures for disease prevention and treatment. Our findings suggest that more focus of public health is needed to prevent the outbreak of infectious diseases in colleges.

Materials and methods

Study participants

There were 656,212 freshmen attending 30 colleges and universities in Zhengzhou, China, in 2004–2013. This study was conducted in accordance with the ethical standards of the Helsinki Declaration, and approved by the Medical Ethics Committee of the Sixth People's Hospital of Zhengzhou (document number 2011HNIN003). In accordance with China's national conditions, the main auxiliary method of tuberculosis diagnosis for freshmen was PPD screening. All participants provided verbal consent, and permission was obtained from local authorities.

Tuberculosis testing

Study participants received 0.1 ml (5 IU) PPD (1:2000) subcutaneously in the inner forearm. Forty-eight to 72 hours after injection, the site was evaluated by a physician. The reaction was considered to be negative, weakly positive, moderately positive, and strongly positive with greatest swelling diameters of < 5 mm, 5–9 mm, 10–19 mm and ≥ 20 mm (or < 20 mm with blisters, necrosis or lymphatitis), respectively²⁷.

TB treatment

Students with a strongly positive PPD test result underwent chest X-ray examination. In case of lung shadow discovery upon imaging, the students were referred to the TB Control Institute, Zhengzhou City, for further examination. Students with a strongly positive PPD test result as well as those with undetermined active TB status were administered preventive medication after written informed consent. The two treatment regimens used were isoniazid at 0.3 g/day for 6 months or Rifapentine and isoniazid combination at 0.6 g twice weekly for 3 months²⁸. Confirmed active TB cases were transferred to local TB prevention and control institutions for out-patient or inpatient treatment, and instructed to stay at home for 1 to 3 months. All patients underwent treatment by TB prevention and control institutions until disappearance of clinical symptoms, demonstrated by three consecutive negative sputum smear examinations for *acid-fast bacilli* (AFB) and lung imaging showing no fibrosis or sclerosis. High prevalence of persistent cough and AFB-positive sputum smears required further exploration. Patients with clinical

cure- and restoration class certificates issued by respective TB prevention and control institutions could return to school. The College Hospital Preventive Care Section archived the information of each patient and tracked patient management until recovery.

Statistical analysis

Statistical analyses were performed with SPSS, version 17.0 (SPSS Inc., Chicago, IL, USA). $P < 0.05$ was considered statistically significant. Multiple groups were compared with the χ^2 test.

Results

Of the 656,212 students administered the PPD test, 221,292 (33.72%) and 434,920 (66.28%) lived in urban

and rural areas, respectively; 341,186 (51.99%) were males, with 315,026 (48.01%) females. A total of 266,992 (40.69%) and 44,563 (6.79%) were positive and strongly positive, respectively. There were 960 diagnosed TB cases, indicating an incidence of 146.29/100,000. Over the 10-year study period, the PPD positive rate and TB prevalence increased annually (Fig 1). A comparison of annual weakly positive rates showed a statistically significant difference ($P < 0.0001$); similar results were obtained for moderately positive PPD, strongly positive PPD, and total positive PPD cases, as well as TB prevalence ($P < 0.0001$). The total positive and strongly positive rates, as well as prevalence in boys were significantly higher than the values obtained for girls, and significantly higher in rural than urban areas ($P < 0.0001$) (Table 1).

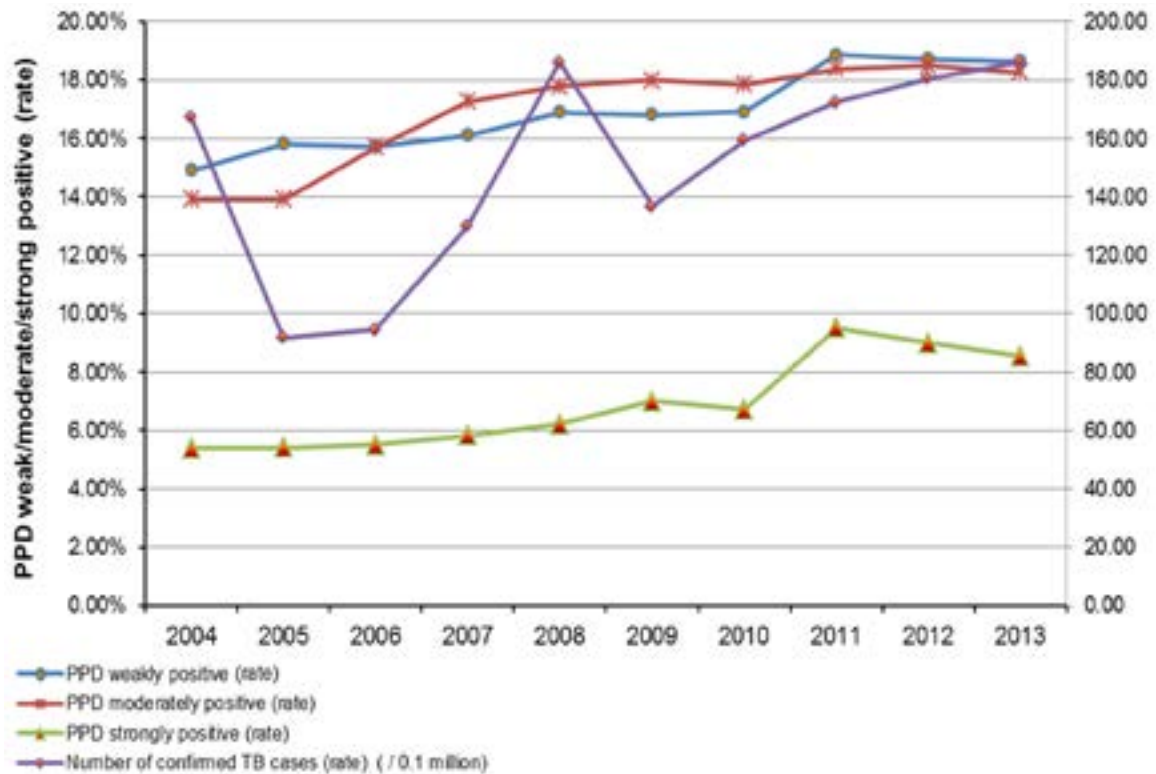


Figure 1 Trend of PPD test results of 2004-2013 freshmen in Zhengzhou City (cases).

Table 1 PPD test results by year

Year	Number of participants	PPD positive								Confirmed TB cases		Number of colleges surveyed
		PPD weakly positive		PPD moderately positive		PPD strongly positive		Total positive		N	/100,000	
		N	%	N	%	N	%	N	%			
2004	45,437	6,775	14.91	6,316	13.90	2,445	5.38	15,536	34.19	76	167.30	4
2005	54,459	8,610	15.81	7,575	13.91	2,941	5.40	19,126	35.12	50	91.80	5
2006	65,576	10,302	15.71	10,289	15.69	3,607	5.50	24,198	36.90	62	94.50	6
2007	97,673	15,735	16.11	16,858	17.26	5,684	5.82	38,277	39.19	127	130.00	8
2008	70,940	11,989	16.90	12,613	17.78	4,405	6.21	29,007	40.89	132	186.10	7
2009	101,578	17,075	16.81	18,264	17.98	7,110	7.00	42,449	41.79	139	136.80	9
2010	82,776	13,997	16.91	14,767	17.84	5,564	6.72	34,328	41.47	132	159.47	7
2011	87,585	16,519	18.86	16,098	18.38	8,331	9.51	40,948	46.75	151	172.40	7
2012	42,676	7,989	18.72	7,887	18.48	3,834	8.98	19,710	46.19	77	180.43	4
2013	7,512	1,399	18.62	1,372	18.26	642	8.55	3,413	45.43	14	186.37	1
The total	656,212	110,390	16.83	112,039	17.07	44,563	6.79	266,992	40.69	960	146.29	

As shown in Figure 1, the rate of confirmed TB cases peaked in 2008, because a high school and a university in Zhengzhou failed to perform PPD tests in 2007, with a TB outbreak in these institutions occurring in 2008. In addition, 2013 marked the final rising trend in total number of confirmed TB cases, because only one university in Zhengzhou performed TB surveillance due to a shortage of funds. We also noticed that many colleges had not administered PPD tests for nearly two years in Henan province.

PPD test results by gender and region

A total of 41.68% males had positive PPD results, with a prevalence of 218.65/100,000. Meanwhile, 39.61% females had positive PPD results, with a prevalence of 67.93/100,000. Total positivity rate, strongly positive rate, and TB prevalence were all significantly higher in males than in females ($p < 0.0001$). Total positivity and prevalence rates in urban students were 38.03% and 80.44/100,000, respectively, while rural students had rates of 42.04% and 179.80/100,000, respectively. Total positivity, strongly positive, and prevalence rates were significantly higher in rural students compared with urban counterparts ($p < 0.0001$) (Table 2).

Table 2 PPD test results by gender, and residence location among study participants

Projects	Sample size	Number of PPD positive (rate)								Number of confirmed	
		PPD weakly positive		PPD moderately positive		PPD strongly positive		Total positive		TB cases	/100,000
		N	%	N	%	N	%	N	%		
Male	341,186	56,777	16.64	59,672	17.49	25,754	7.55	142,203	41.68	746	218.65
female	315,026	53,613	17.02	52,367	16.62	18,809	5.97^a	124,789	39.61	214	67.93^b
The total	656,212	110,390	16.83	112,039	17.07	44,563	6.79	266,992	40.69	960	146.29
Urban	221,292	36,435	16.47	38,286	17.30	9,426	4.26	84,147	38.03	178	80.44
Rural	434,920	73,955	17.00	73,753	16.96	35,137	8.08^c	182,845	42.04	782	179.80^d
The total	656,212	110,390	16.83	112,039	17.07	44,563	6.79	266,992	40.69	960	146.29

Note: Compared to boys, **a** = 537.38, $P < 0.001$; **b** = 254.70, $P < 0.001$. Compared to rural, **c** = 3380.17, $P < 0.001$; **d** = 99.13, $P < 0.001$.

Discussion

This study revealed an increase in the prevalence of PPD positivity over 10 years, corroborating other reports in China^{29,30}, but different from the decreasing trend found in the 2010 FNTES.

College freshmen are active and mobile, increasing the risk of TB transmission. A large number of young adult TB cases constitute an obstacle to TB control³¹. College students undergo physical development and endocrinological changes from adolescence to adulthood, with poor dietary behaviors and less physical activity, which affect long-term health and chronic disease risk³².

The students examined had just completed the college entrance examination (CEE), with elevated stress and possibly a weakened immune system. They tended to have less sleep, lived in cramped dormitories, and studied in classrooms with inadequate air quality. Some had poor nutrition, which further contributed to immune suppression. Such factors increase the risk of contracting TB.

Students attending university are required to undergo entrance physical examination and PPD test. With PPD examinations in freshmen, TB epidemic rarely occurs. However, a senior middle school and a university in Zhengzhou in 2007 failed to perform PPD testing, and a TB outbreak occurred at the two institutions. This emphasizes the importance of TB screening in this vulnerable population.

Analysis of PPD test results in boys and girls

Total and strongly positive rates, and the prevalence of positive PPD results in study participants were significantly higher in men compared with women, as previously reported in China³³. A potential factor contributing to this difference is that males frequent internet cafes more often than females; these cybercafés tend to be crowded, with poor ventilation. Another possible reason is the poorer hygiene in men's dormitories compared with women's, making TB transmission more likely. TB transmission is related to long-term close contact and a dirty living environment³⁴. In many low- and middle-income countries women smoke less than men³⁵, and smoking increases the risk of pulmonary tuberculosis³⁶.

Comparison of PPD test results between urban and rural students

Our survey demonstrated that total and strongly positive PPD results, as well as TB prevalence were higher in students from rural regions than those from urban areas. Poor economic conditions and nutritional deficiencies in rural areas may lead to lower immunity. Some poor students from rural areas can only afford basic needs, and may have inadequate intake of meat, eggs, milk and fruits. Rural students may also have less knowledge regarding TB control because health education only comprises a few lectures per semester in many high schools. The lack of basic knowledge of hygiene can result in bad habits such as spitting, which increases the risk of TB transmis-

sion. We suggest health education should be provided to students from primary school through university.

Therapeutic measures for individuals with strongly positive PPD tests

Students with strongly positive PPD results, i.e. who have latent TB infection, should be educated about the importance of treatment, and treated to prevent transmission. PPD negative students should be injected BCG vaccine for protection against TB. Strongly positive PPD test students should be immediately treated. According to WHO more than a decade ago, the most cost-effective way to stop TB in communities with high incidence is by curing it. DOTS (Directly-Observed Treatment, Short-Course) is considered the best curative method for TB³⁷. However, some students find it difficult to conform to unaffordable TB medication with DOTS standards, and to comply with regimens in developing countries. Irregular medication use can lead to TB drug resistance. Therefore, coordinated efforts should target continuous scale-up of screening, early diagnosis, and proper treatment of TB, in line with DOTS. The ultimate goal is effective prevention and control of TB in this high risk population.

Conclusion

A TB control program includes screening, tracking (such as drugs for prophylaxis and treatment) and re-check, and any disrupted link could increase TB prevalence. Therefore, adequate human and financial resources are needed for TB control programs. Direct and indirect costs, as well as social consequences of TB can be devastating to the patient, family and community^{38,39}. Positive PPD rates in the assessed freshmen have increased yearly during the study period. Colleges and the public health department should be aware of this trend and implement adequate measures.

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Conflict of interest

All authors declare that they have no conflict of interests.

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