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ORIGINAL RESEARCH

Predictors of Tuberculosis Preventive Treatment Completion in College Students: A High Adherence Study in China

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Purpose: To investigate and evaluate factors associated with completion of tuberculosis preventive treatment (TPT) among college students with latent tuberculosis infection (LTBI).

Patients and Methods: We conducted a cross-sectional survey of 399 LTBI college students who initiated TPT in Shandong Province, China. TPT completion rates were determined. Factors associated with TPT completion were assessed by multivariate logistic regression analysis.

Results: Of the 399 students initially initiated TPT, 364 (91.2%) eventually completed treatment. Non-medical students were more likely than medical students to discontinue TPT early [adjusted odds ratio (aOR) = 0.31, 95% confidence interval (CI): 0.13–0.78; *E*-value = 1.79). Students with higher family income (aOR = 0.27, 95% CI: 0.12–0.60; *E*-value = 1.94) and higher education levels (aOR = 0.08, 95% CI: 0.02–0.31; *E*-value = 3.48) were less likely to complete the TPT. Students who did not experience adverse reactions during medication (aOR = 9.46, 95% CI: 2.67–33.64; *E*-value = 3.08) were more likely to complete TPT. *E*-value analysis showed robustness to unmeasured confounders.

Conclusion: Standardized medication management is critical to the completion of preventive treatment. To improve TPT adherence, we suggest tailored interventions based on factors associated with TPT completion, such as the individual (type of student, level of education, incidence of adverse events) and family characteristics (household income) of college students with LTBI, are identified as improving LTBI treatment completion.

Keywords: latent tuberculosis, treatment completion, chemoprophylaxis, prevention

Introduction

Tuberculosis (TB) remains one of the major infectious diseases that pose a serious threat to human health.[1] China has one of the highest burdens of tuberculosis (TB) and latent TB infection (LTBI) in the world. According to the latest global TB report released by WHO,[2] China had a TB incidence rate of 52 per 100000 population in 2023, ranking third among the 30 high-burden TB countries. In addition, it was estimated that approximately 350 million people in China were infected with Mycobacterium TB.[3] The LTBI population is like a huge reservoir of active TB. Although they do not transmit the infection, there is about a 5% to 10% risk of eventually developing active TB if left untreated.[4–6] It is now widely recognized that the management of LTBI is as important as active TB in achieving the goals of the End TB Strategy.

TB preventive treatment (TPT) is an effective intervention to prevent progression from LTBI to TB. Several TPT regimens have shown efficacy.[7] However, the efficacy of TPT is usually dependent on patient adherence throughout the treatment period and completion of the entire course of therapy.[8] A systematic review showed that TPT completion rates

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ranged from 4% to 100% for populations including contacts, homeless people, HIV-infected individuals, prisoners, and immigrants.[9] The diversity of treatment regimens, types of at-risk populations, and accessibility of health services affect TPT completion to some extent, resulting in significant differences in TPT completion rates among populations.[9,10] In addition, adherence to TPT is influenced by a variety of factors, with treatment duration and adverse events being well-known impediments to TPT completion.[11,12]

In China, the reported incidence of TB among students is about one-third of the whole population, slightly lower than that of the general public, primarily among high school and college students.[13] Although the TB incidence rate among students is lower than that of the general population, the occurrence of TB in this group may attract more attention and potentially lead to public health events. The high population density and crowded living conditions in schools may facilitate the spread of TB among students and even result in severe outbreaks in the short term. TB outbreaks in schools usually pose a public health threat to students and their families and can have a significant social impact. Therefore, the prevention and control of TB among students have received increasing attention from the Chinese government.

Students with TB tend to have many close contacts, which increases the prevalence of LTBI in schools.[14] Screening and treatment of LTBI in the student population are highly beneficial in reducing the subsequent incidence and transmission of TB. LTBI chemoprophylaxis has been recommended in China for adolescents with a strong positive tuberculin skin test (TST) reaction, and chemoprophylaxis programs have been piloted in several high schools and universities.[15,16] Although LTBI screening strategies and TPT have been promoted, treatment completion is not routinely reported. It is an important indicator of the impact of screening programs, safety, and cost-effectiveness. Acceptance and adherence to completing treatment are equally important. Currently, there is still limited research in China on TPT adherence among student populations. Previous studies have mostly focused on close contacts of patients with active TB, who are likely to have higher treatment adherence due to their high self-perceived risk of exposure.[17,18] The student population, however, may be quite different. Therefore, understanding the barriers and factors associated with LTBI treatment completion will help colleges develop effective and appropriate interventions for the management of LTBI.

The purpose of this study was to investigate treatment completion rates among college students with LTBI who initiated TPT and to identify factors associated with TPT completion.

Materials and Methods

Study Design

This study used data from the TPT assessment program for LTBI college students in Shandong Province, China. The program began in September 2023 and was organized by the Shandong Province Public Health Clinical Center in 18 colleges in 16 cities in Shandong Province. All freshmen entrants to the school are screened for TB infection by the purified protein derivative (PPD) test, symptomatic questioning, and X-ray chest examination.

In April 2024, we conducted a retrospective cross-sectional survey. A simple random sampling method was used to select students who had initiated TPT in the colleges mentioned above. Participants were included according to the following criteria: (1) LTBI was diagnosed by a strong positive PPD (induration diameter≥15 mm or localized double circles, blisters, necrosis, and lymphangitis), (2) active TB and contraindications to treatment had been ruled out, and (3) voluntary acceptance of TPT and signed informed consent. According to the Chinese Guidelines for Preventive Treatment of TB, a 3-month weekly isoniazid and rifapentine combination intermittent regimen (3HP) or Mycobacterium vaccae injection was used.[19] Finally, 399 LTBI students were surveyed, and a questionnaire was completed. All participants gave informed consent. The study was approved by the ethics committee of the School of Public Health, Shandong University (No. LL20200306).

Sample Size Determination

The sample size was determined according to the following formula with a confidence level of 95% (α= 5%) and an allowable error (d) of 0.05. We consider the data referencing TPT for LTBI Dalian students in China, with TPT adherence rates ranging from 64.8% to 90.3%.[20]

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Considering a 10% loss to follow-up rate, the final sample size was determined to be 390.

Data Collection and Definitions

To collect data, the researcher developed a questionnaire based on relevant literature. Survey items were close-ended single-choice questions with predefined response options. The questionnaire was used to obtain the following information: age (continuous), gender (female, male), education level (associate degree, undergraduate degree and above), annual household income (<90000 RMB, ≥90000 RMB), presence of chronic diseases (yes, no), regular exercise (yes, no), family support for treatment (yes, no), adverse reactions during treatment (yes, no), and the status of the TPT completion. All questionnaire data were collected by uniformly trained staff. Treatment completion was defined as ingestion of more than 80% of all prescribed medications without missing visits.

Statistical Analysis

Statistical analyses were performed by R software version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria). Categorical data were described using frequency counts and component ratios. Qualitative data were analyzed using Pearson chi-square test and Fisher's exact test. Multivariate logistic regression analysis was used to assess factors associated with TPT completion. Before multivariate logistic regression analysis, we calculated variance inflation factors (VIF) to check for multicollinearity. Sensitivity analysis of the results was performed using the *E*-value method.[21] All comparisons were two-sided and $P < 0.05$ was considered statistically significant.

Results

A total of 399 LTBI college students who received TPT were investigated in our study. The mean age of the participants was 19.9 ± 0.1 years. There were 210 (52.6%) females and 189 (47.4%) males. More than half of the participants had an education level of undergraduate or higher. 55.9% of the participants' majors were non-medical. 73.9% of the participants had an average annual household income of less than 90,000 RMB. 68.2% of the participants engage in regular physical exercise. Detailed information on other general characteristics is reported in Table 1.

The medication for LTBI students was managed uniformly by the medical staff of the campus hospital. The TPT completion rate was 91.2% (364/399). Among the 35 LTBI students who did not complete the treatment, 7 (20.0%) discontinued due to "adverse reactions" and 28 (80.0%) discontinued due to "personal reasons". Adverse reactions occurred in 21 participants during the treatment. The incidence of adverse reactions was 5.3% (21/399) and the discontinuation rate due to adverse reactions was 1.8% (7/399).

The results of multivariate logistic analysis are shown in Table 2. After adjusting covariates, students with an undergraduate degrees or higher were less likely to complete TPT (aOR = 0.08, 95% CI: 0.02–0.31). This means that students with undergraduate degree or higher had 0.08 times the odds of completing TPT compared to those with lower education, indicating a significant inverse association. Non-medical students had 0.31 times the odds of completing TPT compared to medical students (aOR = 0.31, 95% CI: 0.13–0.78). Students with an average annual household income of 90000 RMB or more were less likely to complete TPT (aOR = 0.27, 95% CI: 0.12–0.60). Students without adverse reactions had 9.46 times the odds of completing TPT compared to those experiencing side effects (aOR = 9.46, 95% CI: 2.67–33.64). The VIFs of the independent variables in the model were all less than 1.5, indicating that there was no multicollinearity among the independent variables. We generated *E*-values to assess sensitivity to unmeasured confounding. The primary findings were robust unless there were unmeasured confounders with OR greater than 3.48 (educational level), 3.08 (adverse reactions), 1.79 (student type), and 1.94 (household income).

Discussion

The clinical benefits for LTBI patients and the success of LTBI control generally depend on the individual's adherence to medication and completion of the entire treatment course.[8] In our study, the TPT completion rate was 91.2%. Direct

Table 1 General and Clinical Characteristics of 399 College Students Receiving Tuberculosis Preventive Treatment

Characteristics	Total N=399 (%)	TPT Completion Status		*P* value
		Completed N=364 (%)	Not Completed N=35 (%)	
Gender				
Male	189(47.4)	173(47.5)	16(45.7)	0.837
Female	210(52.6)	191(52.5)	19(54.3)	
Age group (years)				
<20	324(81.2)	292(80.2)	32(91.4)	0.239*
20–25	62(15.5)	60(16.5)	2(5.7)	
≥25	13(3.3)	12(3.3)	1(2.9)	
Educational level				
Associate degree	160(40.1)	157(43.1)	3(8.6)	<0.001
Undergraduate degree and above	239(59.9)	207(56.9)	32(91.4)	
Type of students				
Medical students	176(44.1)	167(45.9)	9(25.7)	0.022
Non-medical students	223(55.9)	197(54.1)	26(74.3)	
Average annual household income (RMB)				
<90,000	295(73.9)	279(76.6)	16(45.7)	<0.001
≥90,000	104(26.1)	85(23.4)	19(54.3)	
Combined chronic diseases				
Yes	7(1.8)	6(1.6)	1(2.9)	0.477*
No	392(98.2)	358(98.4)	34(97.1)	
Regular exercise				
Yes	272(68.2)	250(68.7)	22(62.9)	0.480
No	127(31.8)	114(31.3)	13(37.1)	
Distance between dormitory and campus hospital				
<500 m	167(41.9)	151(41.5)	16(45.7)	0.628
≥500 m	232(58.1)	213(58.5)	19(54.3)	
Family support for TPT				
Yes	375(94.0)	341(93.7)	34(97.1)	0.710*
No	24(6.0)	23(6.3)	1(2.9)	
Adverse reaction during medication				
Yes	21(5.3)	15(4.1)	6(17.1)	0.006*
No	378(94.7)	349(95.9)	29(82.9)	

Note: *Fisher's exact test was used.
Abbreviations: LTBI, latent tuberculosis infection; TPT, tuberculosis preventive treatment.

comparisons with previous studies are difficult due to differences in study design, regimen, and study populations. TPT completion rates vary by risk group. According to a meta-analysis,[22] TPT completion rates in different populations ranged from 19% to 90%. A retrospective cohort study in the United States showed that only 45% of 15035 patients with

Table 2 Multivariate Analysis of Factors Associated with Completion of the TPT

Variables	Unadjusted Model			Adjusted Model*		
	OR	95% CI	*P* value	aOR	95% CI	*P* value
Gender						
Male	Ref			Ref		
Female	0.93	0.46–1.87	0.837	0.81	0.35–1.81	0.596
Age group (years)						
<20	Ref			Ref		
20–25	3.29	0.77–14.09	0.109	3.43	0.74–15.97	0.117
≥25	1.32	0.17–10.45	0.796	2.80	0.31–25.51	0.361
Educational level						
Associate degree	Ref			Ref		
Undergraduate and above	0.12	0.04–0.41	0.001	0.08	0.02–0.31	0.000
Type of students						
Medical students	Ref			Ref		
Non-medical students	0.41	0.19–0.89	0.025	0.31	0.13–0.78	0.010
Average annual household income (RMB)						
<90000	Ref			Ref		
≥90,000	0.26	0.13–0.52	0.000	0.27	0.12–0.60	0.001
Combined chronic diseases						
Yes	Ref			Ref		
No	1.76	0.21–15.01	0.607	0.37	0.01–15.71	0.600
Regular exercise						
Yes	Ref			Ref		
No	0.77	0.38–1.59	0.481	0.51	0.22–1.20	0.124
Distance between dormitory and campus hospital						
<500 m	Ref			Ref		
≥500 m	1.19	0.59–2.39	0.628	2.13	0.94–4.83	0.071
Family support for TPT						
Yes	Ref			Ref		
No	2.24	0.30–17.51	0.424	1.72	0.18–16.97	0.641
Adverse reaction during medication						
Yes	Ref			Ref		
No	4.81	1.74–13.35	0.003	9.46	2.67–33.64	0.001

Notes: *Adjustments were made for gender, age, education level, student type, household income, chronic diseases, regular exercise, distance to the campus hospital, family support, and adverse reactions.

Abbreviations: LTBI, latent tuberculosis infection; TPT, tuberculosis preventive treatment; Ref, reference; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval.

LTBI, including immigrants, HIV-infected individuals, contacts, and homeless people, completed prophylaxis.[23] The study by Michelle et al showed that among LTBI patients aged 18–49 years, the completion rate of the 3HP regimen was 79%.[24] Despite the different levels of adherence, LTBI students in our study had significantly higher TPT completion rates. This may be attributed to the fact that the medication administration methods were all centrally administered by the

medical staff in the school hospital. Appropriate follow-up management of TPT is crucial, and we recommend that the centralized management model by healthcare professionals be replicated in other colleges, combined with intelligent management tools, to further enhance adherence.

After adjusting for other confounding variables, our study found that LTBI students with higher levels of education were more likely to end treatment early. This finding is inconsistent with previous studies.[25] A similar pattern was found in a related study on TPT acceptance rates among healthcare personnel, with doctoral-level physicians and scientists having the lowest treatment acceptance rates.[26] This inconsistent finding suggests that this group may have specific concerns about TPT. The possible explanation is that students with higher education levels may be more concerned about the prolonged duration of TPT, unobservable long-term effects, and the potential side effects. This concern makes it difficult for them to continue to complete TPT. In the treatment process, this group may need to be informed not only about public health recommendations but also about the scientific data that underpin the effectiveness of the treatment program. This approach could be integrated into college health policies and treatment protocols to improve adherence and ensure better treatment outcomes.

Non-medical students were associated with an increased likelihood of interrupted TPT compared to medical students. One possible explanation is that non-medical students lack important TB knowledge and lack a comprehensive understanding of TB and LTBI.[27,28] Although we provided health education related to TB knowledge to the students prior to TPT initiation, it may not have ultimately impressed the non-medical students. In addition, non-medical students may have misconceptions about TB and LTBI. They have a lower perceived risk of LTBI progressing to TB. Colleges should consider appropriately increasing the frequency of health literacy for non-medical students. Individualized approaches focused on increasing beliefs about the disease and educational programs for disease perception correction may be helpful in improving treatment adherence.

In our study, LTBI college students with higher family incomes were more likely to discontinue TPT. This is consistent with previous studies.[16] A survey of adult household contacts of TB patients in India also found that lower economic level was a predictor of receiving TPT.[29] One possible explanation is that students with higher family incomes may have more health coverage, perceive a lower disease burden, and not feel the need to follow a strict treatment plan. Another possible explanation is that, in this survey, the provision of free drugs and examinations had less incentive effect on students from better-off families compared to those from less well-off families. LTBI college students from low-income families often worry about the added financial burden of illness on their families. Therefore, we suggest that it is necessary to provide incentives for different populations during the treatment process.

We found that adverse effects were an important factor leading to treatment discontinuation, even if the criteria for early termination were not met. This finding is consistent with the results of other studies assessing the impact of adverse effects on TPT adherence.[30–32] As the treatment is prophylactic rather than therapeutic, mild to moderate side effects may affect the patient's motivation to continue treatment.[11,33] Therefore, the ability of healthcare providers to recognize and manage adverse effects in a timely manner, coupled with psychological counseling and support, is necessary to improve treatment adherence.

A limitation of this study is that we lacked more detailed information about the reasons why students discontinued TPT, which will be further explored in future studies. Since some participant characteristics were self-reported by the students, recall bias may have affected the accuracy of the results. In addition, this study has selection bias, as the sample consists of students who voluntarily participated in the treatment and may have higher health awareness than non-participants. This bias may affect the generalizability of the results. Finally, the scope of this study was limited to Shandong Province and did not cover other regions or countries, and the results cannot be generalized due to the limitations of different social and cultural contexts.

Conclusion

This study shows that a high completion rate of TPT is also possible through well-organized medication supervision and management. Understanding the factors associated with TPT completion rates is critical to assessing the effectiveness of screening LTBI strategies. Our findings indicate that factors such as type of specialty, level of education, adverse reactions, and family income were associated with LTBI students' completion of treatment. Therefore, we recommend

that policymakers, college health services, and TB prevention programs consider these factors when developing interventions. To improve TPT completion rates, it is critical to develop the capacity to individualize interventions and strengthen the monitoring of adverse reactions. In addition, policy support and investment of resources will help optimize the implementation and effectiveness of TPT.

Ethical Approval

Our study complied with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the School of Public Health, Shandong University (number LL20200306).

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Disclosure

The authors report no conflicts of interest in this work.

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