Preplanned Studies

Epidemiological Characteristics of Rifampicin-Resistant Tuberculosis in Students — China, 2015–2019

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Summary

What is already known about this topic?

The number of students with tuberculosis (TB) has been increasing since 2015. However, the prevalence of rifampicin-resistant tuberculosis (RR-TB) among student population is unclear.

What is added by the report?

The number of students with RR-TB has significantly increased from 2015 to 2019, especially in the western region of China. The majority of patients were college students. Students with RR-TB were mainly new patients.

What are the implications for public health practice?

The following measures are recommended: strengthening TB surveillance in schools, promoting the application of convenient and rapid molecular drug susceptibility testing tools, and actively carrying out drug resistance screening and follow ups for cohabiting children of adult RR-TB patients.

Rifampicin-resistant tuberculosis (RR-TB) is defined as having any resistance to rifampicin, including mono-resistance, multidrug resistance (MDR), and polydrug resistance (*1*). RR-TB is a more serious type of tuberculosis (TB) and is currently the focal point of TB control in China. Students are of special concern for TB control, as once a case of infectious TB occurs, it is easily spread, which will cause public health events and arouse widespread concern in the community. To strengthen the control and prevention of TB among students, the *Guidelines for the Control and Prevention of Tuberculosis in Schools (2017 Edition)* was issued and the single-case early warning system for TB in schools was launched with the China Infectious Diseases Automated-Alert System in July 2018 (*2*). Therefore, although the absolute size of the national TB epidemic is shrinking year by year, the number of the TB cases in schools have grown since 2015 (*3*–*4*). In addition, the prevalence of students with RR-TB is still unclear because of a lack of information on the national drug resistance baseline among children under 15 in the student population. Therefore, it is imperative to analyze the characteristics of the RR-TB epidemic among students.

The Programmatic Management of Drug-Resistant Tuberculosis (PMDT) was initiated in China in 2006. In order to achieve the End TB Strategy's vision and goals proposed by the World Health Organization (WHO) in 2015, China rapidly scaled up coverage of PMDT and expanded the drug resistance screening population for Rifampicin-resistant (RR) from screening high-risk groups of RR-TB to screening all bacteriologically-confirmed TB patients since 2015. The number of RR-TB patients notified after 2015 can better reflect the trends of RR-TB. Therefore, based on the nationwide Tuberculosis Information Management System (TBIMS), this study analyzed the epidemiological characteristics of RR-TB patients registered as students in the occupational classification in the TBIMS from January 1, 2015 to December 31, 2019.

The analysis results showed that the number of students with RR-TB that were reported and the detection rate of RR-TB among student TB patients continued to increase year by year from 2015 to 2019. The number of patients in 2019 was 3.7 times that of 2015 (732 compared to 197), which was higher than the 1.4 (47,732/34,260) times increase of students with TB in the same period. The most significant increase was observed in the western region. Since 2017, the proportion of RR-TB patients has surpassed that of the central and eastern region, ranking first, while the proportion was relatively low in the previous two years (Table 1). The proportion of students with RR-TB in all RR-TB patients also increased year by year (Figure 1).

From Table 1, the number of students with RR-TB notified was predominantly male. The RR-TB patients were mainly college students, followed by high school students. The fewest were primary school patients, with less than 20 cases reported in the 5-year period. Although college students notified the most patients,

TABLE 1. The number of student with TB and with RR-TB, classification of registration and distribution of sex, education level and region of students with RR-TB in China, 2015–2019

Item	2015	2016	2017	2018	2019	Total
No. of students with TB	34,260	36,094	40,656	48,289	47,732	207,031
No. of students with RR-TB (%)*	197 (0.6)	274 (0.8)	383 (0.9)	546 (1.1)	732 (1.5)	2,132 (1.0)
Classification of registration						
New cases (%)	116 (58.9)	180 (65.7)	253 (66.1)	398 (72.9)	570 (77.9)	1,517 (71.2)
RR-TB high-risk groups (%)	81 (41.1)	94 (34.3)	130 (33.9)	148 (27.1)	162 (22.1)	615 (28.8)
Sex						
Male (%)	115 (58.4)	157 (57.3)	201 (52.5)	319 (58.4)	420 (57.4)	1,212 (56.8)
Female (%)	82 (41.6)	117 (42.7)	182 (47.5)	227 (41.6)	312 (42.6)	920 (43.2)
Age						
Primary school: 6–12 years (%)	0 (0)	0 (0)	1 (0.3)	9 (1.6)	9 (1.2)	19 (0.9)
Middle school: 13–15 years (%)	0 (0)	5 (1.8)	6 (1.6)	27 (4.9)	65 (8.9)	104 (4.9)
High school: 16–18 years (%)	9 (4.6)	14 (5.1)	45 (11.7)	103 (18.9)	257 (35.1)	428 (20.1)
University: ≥19 years (%)	186 (94.4)	255 (93.1)	330 (86.2)	407 (74.5)	403 (55.1)	1,581 (74.2)
Region						
East (%)	85 (43.1)	102 (37.2)	125 (32.6)	173 (31.7)	248 (33.9)	733 (34.4)
Central (%)	50 (25.4)	107 (39.1)	122 (31.9)	151 (27.7)	218 (29.8)	648 (30.4)
West (%)	62 (31.5)	65 (23.7)	136 (35.5)	222 (40.7)	266 (36.3)	75 1(35.2)

Note: High-risk groups refer to at least one of the following: (a) chronic TB patients /failure of retreatment TB patients; (b) close contact with a known RR-TB patient; (c) new TB patients of initial treatment failure; (d) relapsed or returned TB patients; or (e) new TB patients with remaining sputum culture or positive smear at the end of the second month after treatment. The ages of students were divided into primary school, middle school, high school, and university categories according to the ages of 6–12, 13–15, 16–18, and 19 years and above. The eastern region included the following provincial-level administrative divisions: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan; the central region: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan; and the western region: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Tibet (Xizang), Shaanxi, Gansu, Qinghai, Ningxia, and Xinjiang.

* Detection rate of RR-TB among student TB patients.

Abbreviations: TB=tuberculosis, RR-TB=rifampicin-resistant tuberculosis.

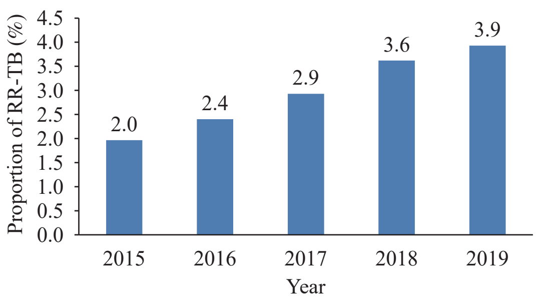

FIGURE 1. The proportion of students with rifampicin-resistant tuberculosis (RR-TB) among all RR-TB patients in the same period in China, 2015–2019.

their proportion decreased year by year, from 94.4% in 2015 to 55.1% in 2019. At the same time, the proportion of RR-TB patients in middle schools and high schools increased year by year, especially in high schools. The increases in students with RR-TB in 2019 were mainly from middle schools and high schools, and the same patients from universities decreased slightly. The majority of students with RR-TB were new patients (71.2%) with no history of TB treatment or treatment duration less than 1 month. The proportion of new patients to the total number of patients increased year by year, from 58.9% in 2015 to 77.9% in 2019. The number of RR-TB patients reported monthly did not show obvious trends (Figure 2).

DISCUSSION

The analysis indicated the number of students with RR-TB increased significantly during 2015–2019 and especially after 2017. This is likely explained because China has successively introduced regulations and early warning measures for the management of TB in schools, which has led to an increase in TB reporting and a corresponding increase in the reported number of students with RR-TB. The increase in students with RR-TB being much higher than students with TB is

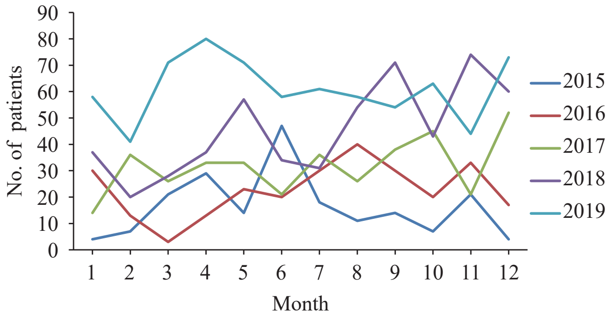

FIGURE 2. Time distribution of the number of students with rifampicin-resistant tuberculosis (RR-TB) reported in China, 2015–2019.

likely related to the rapid increase in RR screening rates, especially the screening rate of new patients after 2015 (*5*).

The number and composition ratio of student RR-TB cases in the western region both increased in 2015–2019. The main reason for this is that the number of students with reported TB and the RR rate in the western region were higher than those in the eastern and central regions (*3*), the number of RR-TB patients in the western region should be the largest. From 2015 to 2018, the Chinese government invested about 260 million CNY to support economically underdeveloped areas, including the western region, to equip drug susceptibility testing (DST) equipment (*6*). Since it will take time for the equipment to be operational, the ability of laboratory personnel to be improved, and an overall increase in DST capacity, fewer students with RR-TB were detected in 2015–2016 compared to the significant increase post-2017.

This study implied that despite the significant increase in students with RR-TB notified from 2015 to 2019, the RR-TB epidemic among primary and secondary school students was underestimated. There are several possible reasons. First, there were few RR-TB cases reported in primary schools at less than 20 cases in 5 years. It is more difficult to detect RR-TB in children compared with adults due to an immature immune system and a difficulty in collecting sputum samples. As a result, there were extremely limited baseline data on TB drug resistance in children in many countries worldwide. According to the estimation of mathematical models, there were 25,000 cases of children in the world with multidrug resistance TB alone. India, China, and Russia, which rank top three in RR-TB cases, accounted for about 7,000 cases (*7*). Therefore, the current data likely underestimates the true situation, and the epidemic of drug resistance in children under 15 in China is likely also underestimated. Second, the rate of RR in high school students should be consistent with that of adults. In 2018, the number of high school students with TB was 1.2 times as high as college students (*3*). However, the number of RR-TB reported in high schools was only one-quarter that of college students. Although the number of notified high school students with RR-TB increased significantly in 2019, the number of college students with RR-TB was 1.5 times higher than that of high school students (403/257). Therefore, the RR-TB notified among high school students was also likely lower than the actual level.

Another issue was that most students with RR-TB were new TB cases, and the proportion of new patients increased year by year. Even in 2015–2017, the screening rate of RR among new TB patients was only about 30% (*5*), the proportion of students with new RR-TB was far higher than that of high-risk groups of RR-TB. In 2019, this proportion was close to 80%, far exceeding the proportion of 54.8% being new cases among all RR-TB patients (*8*). Patients with new RR represent primary drug resistance, so RR-TB among Chinese students was mainly caused by transmission.

The study was subject to some limitations. A more significant feature of student RR-TB cases was that they were prone to clustering. For example, two outbreaks of RR-TB in schools were notified in 2017 and 2019 (*9–10*). Our data source was TBIMS, which cannot yet identify whether student RR-TB patients were from the same school. Therefore, our study did not analyze students with RR-TB clustered epidemics. In addition, there were still some student RR-TB cases, especially those cases under the age of 15 that are not notified in TBIMS, which need to be investigated and analyzed further.

In conclusion, the number of students with RR-TB notified increased significantly in 2015–2019. There was still gap in the detection of students with RR-TB, and students with RR-TB were mainly caused by transmission. In order to reduce the spread of RR-TB in schools and especially to prevent the occurrence of clustered RR-TB outbreaks, the ability to detect RR-TB should be improved and RR-TB should be detected as early as possible. Therefore, it is recommended to strengthen the surveillance of TB in schools, promote the application of convenient and rapid molecular DST tools, and actively carry out drug resistance screening and follow ups for cohabiting children of adult RR-TB patients.

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