Research article

Epidemic characteristics and drug resistance of tuberculosis in North China

Zheng Qi a,1, Xi Gao a, Yan-fu Wang b,1, Chang Liu a,∗

a Engineering Research Center for Medicine, Harbin University of Commerce, Harbin, 150076, China
b Institute of Multidrug-resistant Control, Heilongjiang Province Center for Tuberculosis Control and Prevention, Harbin, 150030, China
c Infectious Disease Department, First Affiliated Hospital of Harbin Medical University, 150001, China

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ABSTRACT

To analyze the epidemiological characteristics and drug resistance of tuberculosis (TB) patients in northern China. The epidemiological characteristics of 620 patients with tuberculosis from 2014 to 2016 were analyzed, including gender, age, occupation, education, income, place of residence and time distribution. 148 strains were identified as mycobacterium tuberculosis infection, 46 of 148 strains were identified as resistant strains, and among which 73.91% of mono-resistance rate, 17.39% of poly-resistance rate, and 8.70% of multidrug resistant rate. Most of the patients were male, farmers, and the age of between 40 and 60, primary education background, income of 5000-10000RMB/year and newly diagnosed patients. The resistance rates of the four first line anti-tuberculosis drugs ranked as S (streptomycin) > R (rifampicin) > H (isoniazid) > E (ethambutol). 12 drug resistance spectrums were found, among them, mono-resistance was mainly concentrated in S (45.65%), poly-resistance was mainly concentrated in H + S (8.70%), and multidrug resistance was mainly concentrated in H + R (4.35%). Therefore, middle-aged people, male, farmers, education for elementary or junior high school, and new patients with incomes not exceeding 10000RMB/year will be the key population for prevention and control in the future and the main drug-resistant population. This is particularly relevant for controlling infection sources, community prevention and control, and drug resistance treatment.

1. Introduction

Tuberculosis is one of the major infectious diseases in the world. In 2016, the number of new cases of tuberculosis in the world was 10.4 million cases and 1.4 million of that were deaths [1]. The phenomenon of drug resistance and multidrug resistance has become increasingly serious. The national multidrug resistance rate of patients with pulmonary tuberculosis was 8.32% based on survey of drug resistance in China during 2007–2008 [2]. In 2015, there were an estimated 580,000 multidrug resistant (MDR) cases globally. Among them, India, China and the Russian Federation accounted for 45% of the total cases of MDR [3]. According to the 2016 World Tuberculosis Annual Report issued by the World Health Organization, China already ranked the third in the world for tuberculosis incidence [4]. Among the 37 statutory reports of Class A infectious diseases in China, tuberculosis cases ranked second, the number of deaths also ranked second [5]. Tuberculosis has become an important public health problem that threatens human health. To reduce the tuberculosis incidences and MDR cases in China, it is important to understand the epidemiological characteristics of tuberculosis and the status of MDR. Monitoring and analysis of tuberculosis incidence and MDR in gender, age, occupation, educational level, income, residence location and timescale was significant important to relative prevention policy put into force [6].

2. Materials and methods

2.1. Data sources

From January 2014 to December 2016, a total of 620 active tuberculosis patients in Binxian county, Harbin city, Heilongjiang province, registered in the TB Network Special Reporting System. The annual population information is derived from the Harbin Statistical Yearbook (http://www.harbin.gov.cn/col/col39/index.html). Active tuberculosis includes: (1) negative tuberculosis; (2) positive for tuberculosis; (3) positive for re-treatment tuberculosis. The identified resistant strains were from mycobacterium tuberculosis in sputum of active patients with suspected tuberculosis. The strains were isolated and cultured from active sputum specimens. Identification of drug-resistant strains after

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drug sensitivity test and collection, drug resistance data was manually entered. Epidemiological data on morbidity, gender, age, occupation, education, income, place of residence and timetable for tuberculosis patients obtained from questionnaires.

2.2. Research methods

The samples collection, transport and test process were according to the Guidelines for the detection of drug resistance in tuberculosis. The acid-fast staining microscopic examination of sputum smears was used, all isolated positive strains samples were to send to the tuberculosis laboratory of Heilongjiang Province Tuberculosis Prevention Center for secondary passage, and bacterial identification performed at the same time. The fresh strains identified as mycobacterium tuberculosis identified according to the operational procedures of the Bacterial Test for the Diagnosis of Tuberculosis [2] and the proportional sensitivity test performed. Mycobacterium tuberculosis was determined by colony morphology, niacin test and nitrate reduction test. There were 4 categories of patients, which including patients of positive sputum smear at the end of 2- or 3-months treatment, patients of initial treatment failure, relapsed patients and patients of failed retreatment were collectively referred to as high-risk groups of tuberculosis resistance. Finally, 148 of 620 people were identified as mycobacterium tuberculosis infection, and drug susceptibility test was conducted. The first-line drugs for drug sensitivity testing in this study were isoniazid (H), rifampicin (R), ethambutol (E) and streptomycin (S). The second-line drugs were ofloxacin (OFX), amikacin (KAM), capreomycin (CPM), propylthiobisobutylamine (PTO), paraamino salicylate (PAS). All positive culture strains were sent to the provincial reference laboratory for drug susceptibility testing. Drug susceptibility testing of these strains was performed as recommended by WHO/IUATLD (International union for tuberculosis and lung disease), which using four first-line anti-TB drugs and five second-line anti-TB drugs. The final concentrations of drugs in Lowenstein-Jensen media, and the strain was considered to be resistant to the specific drug when the growth rate was >1% compared to the control group (without any drugs). The MDR-TB strains were defined as resistant to both INH and RFP [7]. The technical roadmap was in Figure 1.

2.3. Quality control

Before the investigation, train participants who participated in all sites to conduct training and standardize the uniform standards, investigation methods and techniques. The training content includes the basic information of the patients included, sputum specimens, sputum smear examination, mycobacteria isolation and culture examination, and culture medium monoresistance.

2.4. Related drug resistance definitions

Total drug resistant [8] proportion refers to the percentage of any one or more drug-resistant strains of drug-resistant and drug sensitivity test among all the tested strains. Mono-resistance (MR): resistance to one first-line anti-TB drug only, Poly-resistance (PDR): resistance to more than one first-line anti-TB drug, other than both isoniazid and rifampicin, Multidrug resistance (MDR): resistance to at least both isoniazid and rifampicin.

2.5. Statistical analysis

Data analyzed by descriptive epidemiological method. First, the incidence of active tuberculosis was calculated. The proportion of incident cases was the ratio of the number of incident cases to the total number of active tuberculosis patients. Next, the gender, age, occupation, educational level, income, residence location and timescale of pulmonary tuberculosis patients in Binxian county from 2014 to 2016 were analyzed. Excel 2016 software used to enter the incident files and statistical data, SPSS 19.0 software used to statistical analysis of data, statistical analysis using \( \chi^2 \) test, \( P < 0.05 \) was statistically significant.

2.6. Ethical approval

This study has passed the ethics committee conformation of Heilongjiang Provincial Tuberculosis Center For Disease Control and Prevention. The ethics committee acceptance number is 2018-002X-001.

3. Results

3.1. Epidemiologic characters

3.1.1. Registration active tuberculosis incidence

There were 620 active tuberculosis patients registered from January 2014 to December 2016. The annual average reported proportion of incident cases was 30.25/100,000. Among them, 472 cases were smear negative, 129 cases were new smear positive, and 19 cases were re-treatment smear positive, the incidence of active tuberculosis reported from 2014 to 2016 decreased year by year. The average reported proportion of incident cases was 42.88/100000 in 2016, and the difference has statistically significant (\( \chi^2 = 6.585, P = 0.037, P < 0.05 \) (Table 1).

3.1.2. Tuberculosis patient's distribution characteristics

There were 431 male patients and 189 female patients, the ratio of male to female was 2.28, which has statistically significant (\( \chi^2 = 94.458, P = 0.019, P < 0.05 \) (Table 2). The proportion of below the 14-year-old and above 90-year-old age groups was lower, and then followed the higher 15 years of age group. The patients aged 40 to 49 and 55–64 years old with high proportion. After the age of 65, the proportion of incident cases out of overall cases gradually decreased. The proportion of active tuberculosis patients in each age group statistically analyzed. All the age groups have statistically significant (\( \chi^2 = 14.613, P = 0.001, P < 0.05 \) (Figure 2).

![Figure 1. Technical roadmap.](image-url)
3.1.3. Location, educational background, occupation and income characteristics

Farmers accounted for 85.16% (528/620) of the total incident cases, followed by students accounting for 5.32% (33/620). The proportion of incident cases of rural areas accounted for 81.13% of the total incident cases (503/620). The distribution of academic qualifications was most in the group with primary school education, accounting for 40.48% of the total incident cases, followed by junior high school education accounted for 34.03%. The annual income was 10,000 to 10,999 RMB (22.74%) and 5000 to 5,999 RMB (18.71%) groups have the most patients (Table 3).

3.1.4. Timescale distribution characteristics

Monthly average reported proportion of incident cases of active tuberculosis were listed in Table 4. The proportion of incident cases of active tuberculosis was highest in March and April each year and decline in May, the incidence of tuberculosis increased slightly in August and September of 2014 and 2016, but continued to decline in August of 2015. The incidence of active tuberculosis was lowest in October (Table 4).

4. Drug resistance analysis

4.1. General conditions of drug-resistant patients

From January 2014 to December 2016, 148 tuberculosis patients complied with the definition of a high-risk group (148/620 = 23.9%) that was resistant to tuberculosis and included the drug susceptibility test. Among 148 patients, 115 were male (77.70%), ranging from 13 to 76 years of age, 40–60 years of age (50.00%), occupations were mostly farmers (87.16%), education was mostly elementary school (43.92%) of the total income was in the range of 5000–10,000 (53.38%), 9.46% had a history of diabetes, and 5.41% had a history of hepatitis B. From the perspective of high-risk groups, the new patients were the most (66.22%) (Table 5).

Table 1. Registered active pulmonary tuberculosis incidence in Binxian county during 2014–2016.

| Year | The population of Binxian | Number of active tuberculosis cases | Number of smear negative cases | Number of new smear positive cases | Number of re-treatment smear positive cases | Registered incidence rate (/100 thousand) |
|------|---------------------------|------------------------------------|--------------------------------|-----------------------------------|--------------------------------------------|------------------------------------------|
| 2014 | 599209                    | 253                                | 192                            | 52                                | 9                                          | 42.88                                    |
| 2015 | 579740                    | 234                                | 187                            | 39                                | 8                                          | 39.66                                    |
| 2016 | 579303                    | 133                                | 93                             | 38                                | 2                                          | 22.54                                    |
| Total| 1758252                   | 620                                | 472                            | 129                               | 19                                         | 30.25                                    |

Table 2. Gender distribution of active tuberculosis patients during 2014–2016.

| Year | Male | Female |
|------|------|--------|
|      | Male population in Binxian | Patient cases | Registered TB proportion of incident cases (/100 thousand) | Female population in Binxian | Patient cases | Registered TB proportion of incident cases (/100 thousand) |
| 2014 | 305597 | 174 | 56.94 | 293612 | 79 | 26.91 |
| 2015 | 298116 | 164 | 55.01 | 281624 | 70 | 24.86 |
| 2016 | 297782 | 93  | 31.23 | 281521 | 40 | 14.21 |
| Total| 901495 | 431 | 47.809 | 856757 | 189 | 22.06 |

Figure 2. Gender and age distribution of active tuberculosis patients during 2014–2016.
4.2. Drug-resistant tuberculosis of high-risk group analysis

The 148 cases were sent to 9 kinds of drug susceptibility test, 12 resistant spectrum combinations were identified. 46 strains were found to be resistant to one or more drugs (Proportion of resistant test strains of 31.08%), Among them, 34 cases were MR (73.91%), mainly S resistant (45.65%); 8 cases were PDR (17.39%), mainly SþH resistant (8.70%); 4 cases were MDR (8.70%), mainly HþR resistant (4.35%). During 2014–2016, there were 15, 14 and 17 patients detected respectively for drug susceptibility test every year. Among different classifications, most patients of drug resistant strains were new patients (86.96%). Out of the 46 drug-resistant strains, the order of the resistance rate of anti-tuberculosis drugs was from high to low was S > R > H = OFX. Different types of patients have different rates of resistance. Among the differences, the order of drug resistance in new patients was S > R > H > OFX; the order of drug resistance in relapsed patients was R = OFX > S = H (Table 6).

5. Discussions

The World Health Organization's 2015 Global TB Control Report presented the incidence of tuberculosis reports globally had been slowly declining year by year since 2010, but the number of cases has also increased year by year as the population has increased [7, 8]. Binxian county as a key prevention and control monitoring area, has a total of 620 active tuberculosis patients from 2014 to 2016. The average annual reported incidence of 35.26/100000, which was decreased year by year.

| Item                          | Category                        | Incidence (proportion of incident cases/%) |
|-------------------------------|---------------------------------|--------------------------------------------|
| Urban and rural areas         | Urban                           | 117 (18.87)                                |
|                               | Rural                           | 503 (81.13)                                |
| Occupation                    | Farmers                         | 528 (85.16)                                |
|                               | Students                        | 33 (5.32)                                  |
|                               | Unemployed/laid-off             | 26 (4.19)                                  |
|                               | Educators                       | 3 (0.48)                                   |
|                               | Transportation personnel        | 1 (0.16)                                   |
|                               | Business service staffs         | 1 (0.16)                                   |
|                               | Retired people                  | 10 (1.61)                                  |
|                               | Business employees              | 9 (1.45)                                   |
|                               | State agencies and institutions staffs | 3 (0.48)                                |
|                               | Others                          | 6 (0.97)                                   |

Table 3. Urban-rural, occupation, educational background and income distribution of active tuberculosis patients during 2014–2016 [n (proportion of incident cases/%)].

Table 4. Distribution of active pulmonary tuberculosis in months during 2014–2016.

| Month | Cases (proportion of incident cases, %) |
|-------|-----------------------------------------|
| 2014  | 22 (3.55) 18 (2.90) 31 (5.00) 35 (5.65) 30 (4.84) 18 (2.90) 12 (1.94) 24 (3.87) 22 (3.55) 9 (1.45) 16 (2.58) 16 (2.58) |
| 2015  | 20 (3.23) 17 (2.74) 27 (4.35) 36 (5.81) 26 (4.19) 24 (3.87) 20 (3.23) 19 (3.06) 11 (1.77) 8 (1.29) 16 (2.58) 10 (1.61) |
| 2016  | 9 (1.45) 13 (2.10) 20 (3.23) 11 (1.77) 10 (1.61) 7 (1.13) 12 (1.94) 12 (1.94) 3 (0.48) 15 (2.42) 13 (2.10) |
| Total | 51 (8.23) 43 (6.94) 71 (11.45) 91 (14.68) 67 (10.81) 52 (8.39) 39 (6.29) 55 (8.87) 45 (7.26) 20 (3.23) 37 (5.97) |

4.2. Drug-resistant tuberculosis of high-risk group analysis

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Of the 620 active tuberculosis patients registered from 2014 to 2016, 431 were males and 189 were females, male: female = 2.28:1. The incidence of male registration was 47.81/100,000, and that of females was 22.06/100,000, which was similar to other reported results [9].

The incidence of the age group of under the 14 years old was relatively low. The patients aged 40 to 49 and 55 – 64 years old were the most. The reported incidence rate of active tuberculosis was increasing with age, and the age of onset of tuberculosis was changing to the old age, which was the current trend of tuberculosis in the world [8]. It may be related to the decline of cellular immune function, nutrition and dietary imbalance, and easy infection in the elderly population [10, 11, 12].

The farmer patients' cases of active tuberculosis registered from 2014 to 2016 was the highest, accounting for 85.16% (528/620) of the total incidence, followed by students accounting for 5.32% (33/620). The reported incidences of retirees, laid-off workers, and employees of enterprises were notably higher than those of other occupations, which was consistent with the occupational distribution of tuberculosis epidemic in Guangxi [13].

The incidence in rural areas accounting for 81.13% (503/620) of the total incidence, which was notably higher than that of urban. The distribution of academic qualifications was most in primary school education, accounting for 40.48% (251/620) of the total incidence, followed by junior high school education. The reported incidence of active tuberculosis appeared a downward trend with income growth. It may be they were lack of the prevention and low awareness, nutritional

### Table 5. Epidemiological characters of high-risk group patients [n (proportion of overall cases/%)].

| Item                      | Category                        | Cases  |
|---------------------------|---------------------------------|--------|
| Gender                    | Male                            | 115 (77.70%) |
|                           | Female                          | 33 (22.30%) |
| Age                       | < 40                            | 43 (29.05%) |
|                           | 40–60                           | 74 (50.00%) |
|                           | > 60                            | 31 (20.95%) |
| Educational background    | Illiteracy and semi-literacy     | 10 (6.76%) |
|                           | Primary school                  | 65 (43.92%) |
|                           | Junior high school              | 49 (33.11%) |
|                           | High school, secondary school    | 19 (12.84%) |
|                           | College, university or higher    | 5 (3.38%)  |
| Medical history           | Diabetes                        | 14 (9.46%)  |
|                           | Hepatitis B                     | 8 (5.41%)  |
| Occupation                | Farmers                         | 129 (87.16%) |
|                           | Students                        | 6 (4.05%)  |
|                           | Unemployed/laid-off             | 3 (2.03%)  |
|                           | Transportation personnel         | 1 (0.68%)  |
|                           | Business employees              | 3 (2.03%)  |
|                           | Retired people                  | 4 (2.70%)  |
|                           | Other                           | 2 (1.35%)  |
| Income                    | < 5000                          | 58 (39.19%) |
|                           | 5000–10000                      | 79 (53.38%) |
|                           | > 10000                         | 11 (7.43%)  |
| Suspicious object registration classification | New patient | 98 (66.22%) |
|                           | Relapsed patients               | 50 (33.78%) |

### Table 6. Drug resistance profiles of active tuberculosis patients [n (proportion of overall cases/%)].

| Item                      | Category                        | New patient | Relapsed patients | Total |
|---------------------------|---------------------------------|-------------|-------------------|-------|
| MR                        | H                               | 3 (6.52%)   | 0 (0.00%)         | 3 (6.52%) |
|                           | S                               | 21 (45.65)  | 0 (0.00%)         | 21 (45.65%) |
|                           | R                               | 6 (13.04%)  | 1 (2.17%)         | 7 (15.22%) |
|                           | OFX                             | 2 (4.35%)   | 1 (2.17%)         | 3 (6.52%) |
| Total                     |                                 | 34 (73.91%) |                   |       |
| MDR                       | H + R                           | 1 (2.17%)   | 1 (2.17%)         | 2 (4.35%) |
|                           | H + R + S                       | 1 (2.17%)   | 0 (0.00%)         | 1 (2.17%) |
|                           | H + R + S + OFX + CPM + PAS     | 1 (2.17%)   | 0 (0.00%)         | 1 (2.17%) |
| Total                     |                                 | 4 (8.70%)   |                   |       |
| FDR                       | S + R                           | 0 (0.00%)   | 1 (2.17%)         | 1 (2.17%) |
|                           | S + H                           | 4 (8.70%)   | 0 (0.00%)         | 4 (8.70%) |
|                           | S + R + E + KAM                 | 0 (0.00%)   | 1 (2.17%)         | 1 (2.17%) |
|                           | R + OFX + KAM                   | 0 (0.00%)   | 1 (2.17%)         | 1 (2.17%) |
|                           | OFX + CPM + KAM                 | 1 (2.17%)   | 0 (0.00%)         | 1 (2.17%) |
| Total                     |                                 | 8 (17.39%)  |                   |       |
| Totality                  |                                 | 40 (86.96%) | 6 (13.04%)        | 46 (100%) |

Of the 620 active tuberculosis patients registered from 2014 to 2016, 431 were males and 189 were females, male: female = 2.28:1. The incidence of male registration was 47.81/100,000, and that of females was 22.06/100,000, which was similar to other reported results [9].

The incidence of the age group of under the 14 years old was relatively low. The patients aged 40 to 49 and 55–64 years old were the most. The reported incidence rate of active tuberculosis was increasing with age, and the age of onset of tuberculosis was changing to the old age, which was the current trend of tuberculosis in the world [8]. It may be related to the decline of cellular immune function, nutrition and dietary imbalance, and easy infection in the elderly population [10, 11, 12].

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The incidence in rural areas accounting for 81.13% (503/620) of the total incidence, which was notably higher than that of urban. The distribution of academic qualifications was most in primary school education, accounting for 40.48% (251/620) of the total incidence, followed by junior high school education. The reported incidence of active tuberculosis appeared a downward trend with income growth. The incidence of tuberculosis went to low-educated and low-income people. It may be they were lack of the prevention and low awareness, nutritional
and dietary imbalance, prone to infection and other factors [14]. By analyzing the time distribution of active cases, the annual spring and early summer seasons were the high incidence of tuberculosis.

The majority of high-risk drug-resistant tuberculosis patients or confirmed drug-resistant tuberculosis patients were males, and mainly farmers, aged 40–60 years old, education mainly in junior and high school, income not exceeding 10000. Therefore, patients with low-education background and low-income pulmonary tuberculosis in elderly male farmers in Binxian county or other county like Binxian county in China or whole world are the main targets of drug-resistant tuberculosis. The results are similar to those of Sun Fusheng [15], Chen Huijuan [16] and other surveys of drug-resistant populations in Heze City, Guizhou Province, Shandong Province, which may be related to the hygienic conditions of this population and the compliance of patients with treatment [17].

The total drug-resistance rate was 31.1% in Binxian county, the MR was 79.91%, the PDR was 17.39%, and MDR was 8.70 %. The number of new patients was the highest drug resistance rate, who failed to treatment were the least. The relapse retreatment failure accounted for 13.7%. Among the 46 patients with drug resistance, the order of resistance to any one of the tuberculosis drugs from high to low was S > R > H > OFX, it was similar to the situation of drug resistance in Shandong Province [18]. The National Baseline Survey Report on Drug Resistance in Tuberculosis (2007–2008) reported drug resistance rank was S > H > R > E > OFX > KAM [19], the order of any resistance rate in Shanxi Province was S > H > R > E > OFX > KAM [20], the drug resistance in Hunan province was ranked as follows: H > R > S > E > OFX > KAM [2]. There are obvious regional differences in specific drug-resistant tuberculosis patients, as the first-line drugs obvious the lowest resistance to E, resulting this drug is not easy to produce resistant strains. The present study also presented that 46 drug resistant strains formed a total of 12-drug resistance combination, of which 5 were multidrug resistance and 3 were poly-resistance resistant. Among the multidrug resistant and poly-resistance resistant populations, the Binxian county was S and S + H are predominant, that is, the HS combination is dominant, which is similar to the results of the surveillance of tuberculosis resistance in Shanxi Province [21]. It also suggests that for the formulation of treatment plans for drug-resistant tuberculosis patients, this feature needs to be taken into consideration and should be as a basis for individualized treatment planning. In addition, most resistant strains were from new patients rather than relapsed patients, probably because people in the region did not pay much attention to tuberculosis prevention, and some people had tuberculosis that was resistant when infected. Therefore, it is especially important to strengthen the prevention and treatment of people who close contacts with tuberculosis in this area.

This study retrospectively analyzes active tuberculosis patients and drug resistance surveillance from January 2014 to December 2016 in Binxian county, Harbin city, Heilongjiang province, and describe the epidemic characteristics. It provides experience in the prevention and treatment of drug-resistant tuberculosis in the relative high-risk places in China or other places in the world, also probe a way to reduce the emergence of drug-resistant tuberculosis patients, save medical resources, accurate treatment, and lay the foundation for the next step in reducing the incidence of national average tuberculosis. The prevention and treatment of tuberculosis has a certain guiding significance. Through genetic testing and network analysis, Yang [22] proved that 73% of the patients were caused by transmission, and 44% of them developed the disease within 1–2 years of infection. The transmission mainly occurred in public places, revealing the early detection and source of infection of drug-resistant tuberculosis. Control, community prevention and standardized treatment are essential.

The drug resistance rate of active tuberculosis patients has been increasing in recent years. The main reasons were: (1) Patients lacked awareness of tuberculosis prevention, poor compliance during treatment, irregular medication, insufficient treatment course, and self-premature discontinuation of medication. (2) Patients discontinued and stopped due to economic and physical adverse reactions to the drug, and did not complete the standard full course of treatment according to the prescribed plan. (3) Primary doctors caused drug-resistant tuberculosis in patients due to inappropriate drug use [21]. Both new and retreated patients are important sources of infection for drug-resistant tuberculosis, which greatly increases the risk of drug resistant tuberculosis transmission. Therefore, it is necessary to adopt an effective treatment plan for patients with tuberculosis, and to let each patient understand the importance of early and appropriate medications throughout the entire course, which is of great significance in preventing the increasing number of drug resistant cases of tuberculosis and controlling them [23].

Early detection of drug-resistant tuberculosis, control of the source of infection, community prevention and control, and regular treatment are of utmost importance. We should continue to carry out dynamic monitoring of tuberculosis resistance. Strengthening the hardware construction and testing capabilities of grass-roots laboratories, and popularize new laboratory technologies in diagnosis and drug resistance. Establish laboratory quality control and laboratory quality assessment systems to ensure the accuracy of sputum smear and sputum culture results [24]. The use of detection [25], to control the prevalence of drug-resistant tuberculosis and drug resistance trends, in order to achieve the purpose of reducing drug resistance of tuberculosis. It is also necessary to use rural areas as the focal point for prevention and control.

It is better to adhere to the principle of early, joint, regular, sufficient, and full-course medication, complete the course of treatment at the prescribed dose, and seriously implement the DOTS strategy. Also it is important to standardize the supervision and management of tuberculosis patients [26]. The relevant government departments pay more attention to prevention and control, strengthen the screening of close contacts, and increase the intensity of health education publicity.

**Declarations**

**Author contribution statement**

Z. Qi: Conceived and designed the experiments; Wrote the paper.
X. Gao: Analyzed and interpreted the data.
Y. Wang: Contributed reagents, materials, analysis tools or data.
C. Liu: Performed the experiments.

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**Competing interest statement**

The authors declare no conflict of interest.

**Additional information**

No additional information is available for this paper.

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