Infection and Drug Resistance

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ORIGINAL RESEARCH

Prevalence of Multidrug-Resistant Tuberculosis in Dalian, China: A Retrospective Study

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Purpose: Multidrug-resistant tuberculosis (MDR-TB) is the cause of serious health and economic burdens worldwide. The present study aimed to explore the initial and acquired drug-resistance rates among TB patients from 2012 to 2019 in Dalian, China. The effectiveness of MDR-TB prevention and control strategies were then evaluated.

Patients and Methods: Drug susceptibility testing (DST) was performed for 6429 diagnosed, culture-positive, *Mycobacterium tuberculosis* (MTB) strains, including 4661 new cases and 1768 previously treated cases. Descriptive statistics were employed to calculate the frequencies and percentages of TB strains, and the average annual growth rates (AAGRs) for each strain were calculated. The Chi-square test was applied to examine the significance of linear drug-resistance trends over time during the study period.

Results: Over the eight-year study period, the percentages of both initial (from 9.01% to 4.82%) and acquired (from 40.85% to 9.09%) MDR-TB cases decreased significantly, AAGRs of 8.55% and 19.32%, respectively. Among new and previously treated TB patients, significant downtrends were observed for the rates of both initial and acquired MDR-TB among young and middle-aged individuals ($P < 0.05$). Additionally, among both new and previously treated TB patients, the percentages of individuals with drug resistance against isoniazid (INH), rifampicin (RFP), ofloxacin (OFX), and amikacin (AMK) decreased significantly ($P < 0.05$) from 2012 to 2019 in Dalian, China.

Conclusion: The initial and acquired multidrug resistance rates exhibited significantly decreasing trends from 2012 to 2019, suggesting that MDR-TB prevalence has been controlled effectively in Dalian, China. The MDR-TB epidemic was reversed in the short term by establishing feasible strategies for detection, diagnosis, treatment, and infection control.

Keywords: TB, initial, acquired, MDR, epidemic

Introduction

Tuberculosis (TB), which is caused by *Mycobacterium tuberculosis*, is the most frequently reported deadly infectious disease worldwide.[1,2] Multidrug-resistant tuberculosis (MDR-TB) is defined as TB that is resistant to rifampicin (RFP) and isoniazid (INH), which are the two most effective first-line anti-TB drugs. MDR-TB remains a global public health crisis and health security threat among humans.[3] An estimated 465,000 new RFP-resistant TB (RR-TB) cases were reported in 2019, 78.0% of which were further diagnosed as MDR-TB; additionally, 3.3% of the newly diagnosed and 17.7% of previously treated TB cases have been classified as either MDR-TB or RR-TB, according to estimates by the World Health Organization (WHO).[1] Approximately 6.0% of MDR-TB cases deteriorate into extensively drug-resistant TB (XDR-TB) which is MDR-TB plus resistance to

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a fluoroquinolone and an injectable agent.[1] Worldwide, only 57% of MDR-TB patients achieve successful outcomes by the end of treatment.[1] Treatment for MDR-TB is associated with physical pain and psychological distress in patients, can result in catastrophic health expenditures for families, and requires long-term, heavy consumption of medical resources by healthcare systems. Therefore, identifying effective strategies for controlling the prevalence of MDR-TB is imperative, especially in those regions with high MDR-TB burdens.

A history of previous TB disease and previous TB treatment are the most important risk factors associated with the development of MDR-TB in China.[4–6] Additionally, a trend towards an increased risk of MDR-TB has been identified for younger, low-income individuals, interrupted TB treatment regimen, experienced TB treatment failure, adverse drug reactions, and non-adherence treatment.[6,7] China has been estimated to be among the top 3 nations worldwide with the highest TB burden and a serious epidemic of MDR-TB.[8,9] Approximately 833,000 (range: 717,000–957,000) new TB cases were estimated in 2019 in China, accounting for approximately 8.4% of total new TB cases worldwide. MDR/RR-TB was diagnosed in 7.1% (range: 5.6%–8.7%) of new cases and 23.0% (range: 23%–24%) of previously treated cases in China.[1,10] Recent reports showed that the rates of MDR-TB ranged from 5.7% to 9.0% among new TB cases and from 26.3% to 33.8% among previously treated cases across different regions of China.[11–14] The incidence of MDR-TB is influenced by the large geographic area, unbalanced regional economies, and the inequality of medical resource distribution, which can make monitoring and controlling the MDR-TB prevalence in China very complicated.[12] Starting in 2006, in collaboration with global partner organizations, China has implemented various measures and supportive policies designed to prevent and control the prevalence of MDR-TB, resulting in great progress in the accurate diagnosis, standardization of treatment, and systematic management of MDR-TB patients.[15]

Dalian, which is located in the Liaoning province of northeast China, occupies an area of 12,574 km^2, with a residential population of 6.95 million, and suffers from a high TB burden. MDR-TB is also a serious public health problem in Dalian, and the initial MDR-TB rate of Dalian reached 9.01% in 2012. Based on the Directly Observed Treatment and Short Course-Plus (DOTS-Plus) initiative, the Global Fund for MDR-TB Prevention and Treatment Project was established in 2012 in Dalian. This project developed strategies for the screening, diagnosis, treatment, and whole-process management of high-risk MDR-TB patients.[16] Additionally, the treatment regimen, recommended by the project, was implemented widely, which includes a 6–8-month intensive phase and an 18–28-month continuation, during which patients are treated with the following anti-TB drugs: amikacin (AMK), capreomycin (Cm), ethambutol (EMB), levofloxacin (Lfx), moxifloxacin (Mfx), cycloserine (Cs), p-aminosalicylic acid (PAS), and protionamide (Pto), among others.[17] With persistent efforts, the MDR-TB incidence decreased until 2015, which is when funding for the Global Fund MDR-TB project ended. Since 2015, the local government has appropriated CNY 15 million (approximately USD 2.14 million) annually for TB prevention and treatment.

The prevalence of initial drug resistance in a specific region has been found to be a sensitive indicator of the efficiency of local TB control.[18,19] Acquired drug resistance, which can be affected by a variety of individual and treatment factors, primarily represents the prevalence of previous or pre-existing drug resistance.[20] Recent studies have shown that the MDR-TB epidemic was primarily caused by exogenous infections, spread predominantly through the community, rather than the endogenous recurrence of infection.[21–24] This finding suggests that the primary driver of MDR-TB spread is the transmission of drug-resistant MTB strains from existing MDR-TB patients rather than the suboptimal management of a previous treatment period,[1,25] which provides us with a theoretical basis for the short-term observation of the MDR-TB epidemic. MDR-TB prevention and control strategies have been implemented for many years in Dalian; however, no relevant evaluations of their effects on MDR-TB prevalence have been performed thus far. This study aimed to analyze the prevalence of MDR-TB among patients with initial and acquired drug resistance across different age groups from 2012 to 2019 in Dalian. In addition to multidrug resistance, single drug resistance rates were also explored. Based on these results, we discussed whether the MDR-TB burden could be controlled using the strategies implemented in Dalian, northeast China, which was beneficial for improving MDR-TB prevention and control in the future.

Patients and Methods

Strategies for MDR-TB Prevention and Control

Drug-susceptibility testing (DST) was performed for active, sputum culture-positive TB patients, and MDR-TB patients were identified. New anti-TB drugs and

individual-based treatments were considered when designing the treatment regimens. Additionally, we established separate inpatient wards and outpatient clinic rooms to prevent and control infection during treatment, in which MDR-TB patients were isolated from other TB patients and the general population. Fixed-dose combination

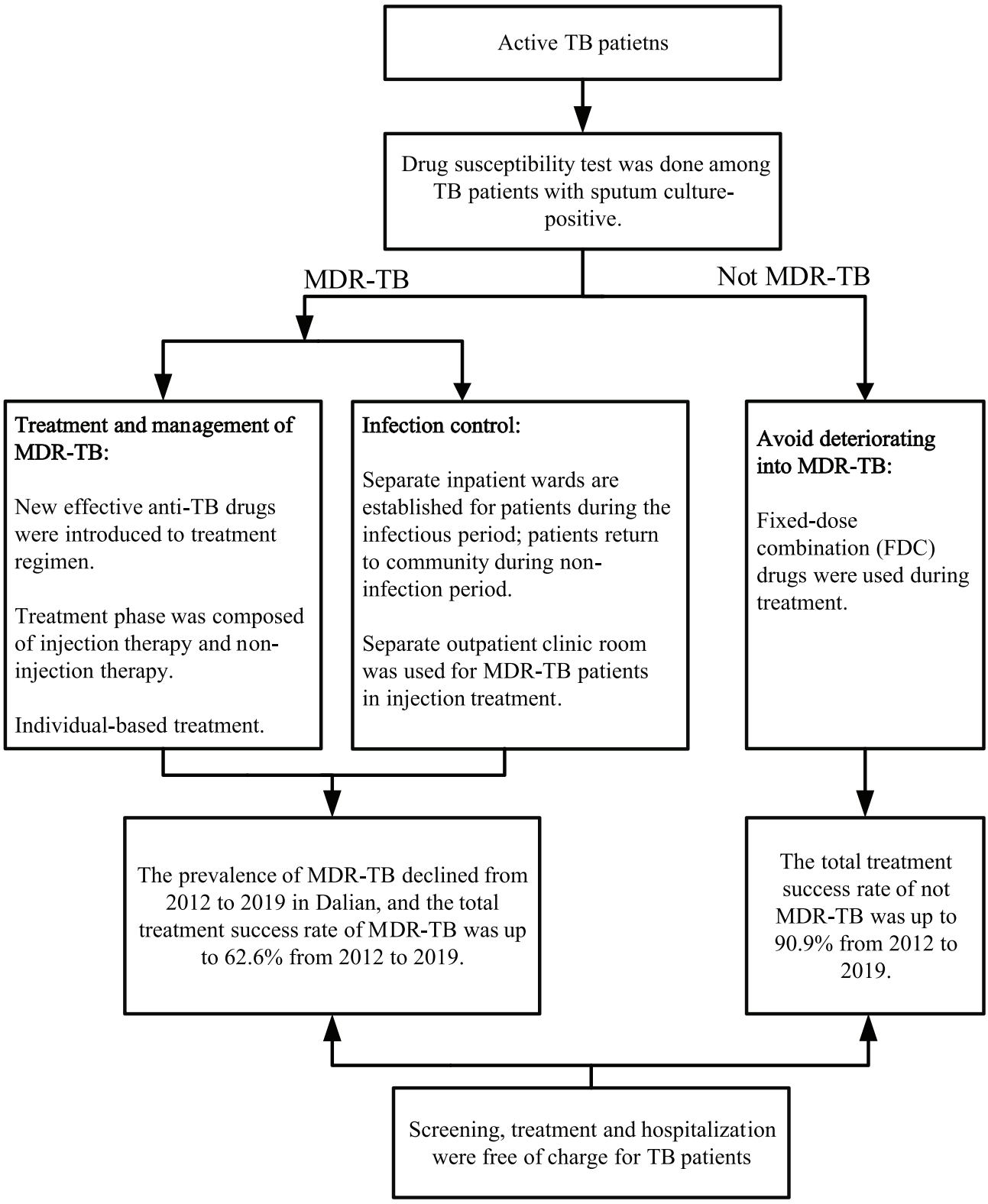

Figure 1 Strategies for the prevention and control of MDR-TB in Dalian.

(FDC) drugs were used among those TB patients without MDR. Screening, treatment, and hospitalization were provided free of charge for TB patients to improve their adherence and willingness to participate in anti-TB treatment.[26,27] As a result, the total treatment success rate for MDR-TB was up to 62.6% from 2012 to 2019 (Figure 1).

Data Collection

Data used in this study were extracted from the China Information System for Disease Prevention and Control, which collects regular information associated with TB surveillance and management. A total of 20,440 newly diagnosed and 2574 previously treated active pulmonary TB cases, from existing databases, were considered for inclusion in this study. All TB cases at the Dalian Tuberculosis Prevention and Control Center of Liaoning Province, China, were reviewed from Jan 1, 2012, to Dec 31, 2019. This center is the only official institution that monitors and treats TB, cultivating more than 90% of TB bacteria in Dalian every year to ensure the accuracy of large sample observations. All MDR-TB cases enrolled in our study were consecutive, culture-confirmed, and underwent DST for first-line anti-TB drugs, including INH, RFP, EMB, and streptomycin (SM), and second-line anti-TB drugs, including OFX and AMK. After data preprocessing, 6429 eligible cases (4661 new cases and 1768 previously treated

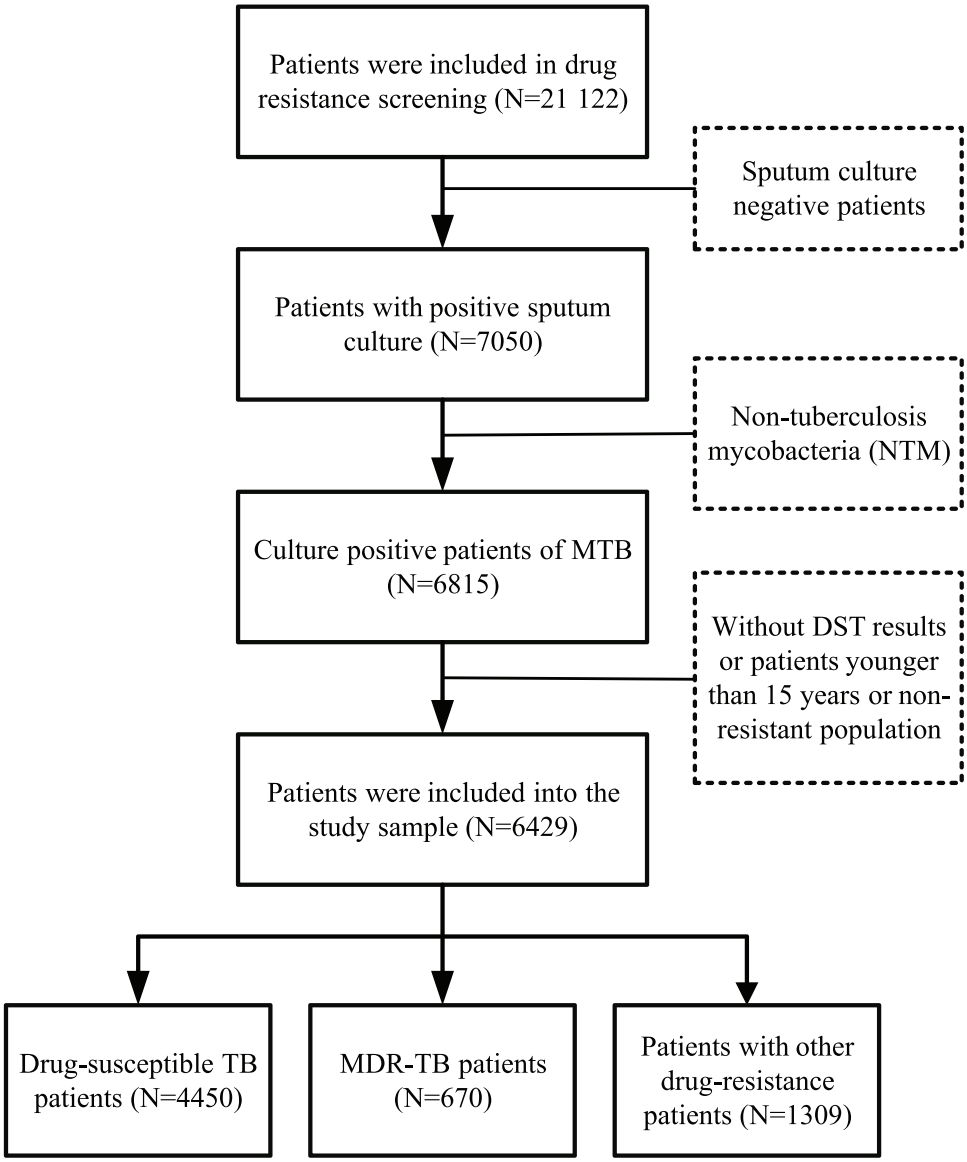

Figure 2 The inclusion strategy applied to select participants in the present study.

cases) were included in the final study analysis, and detail inclusion/exclusion criteria of the participants showed in Figure 2.

Definitions

Patients who were diagnosed with pulmonary TB for the first time, with no anti-TB treatment history or with less than one month of anti-TB treatment history, were considered new cases. Drug-resistant TB strains isolated from these cases were reported as initial drug resistance.[28]

Patients with previous anti-TB treatment that lasted for one month or longer were considered previously treated cases, and drug-resistant TB strains isolated from these cases were reported as acquired drug resistance.[28]

Drug Sensitivity Test

Sputum samples from all patients were collected before the initiation of TB therapy. Samples were cultured in Lowenstein-Jensen medium. A total of 6429 isolates from newly registered TB patients with MTB culture-positive results were subjected to DST against four first-line anti-TB drugs (0.2 μg/mL INH; 40.0 μg/mL RFP; 2.0 μg/mL EMB; and 4.0 μg/mL SM) and two second-line anti-TB drugs (40.0 μg/mL AMK and 4.0 μg/mL OFX) using the proportion method. Strains were considered resistant to drugs when the growth rate exceeded 1% compared with that of the control strain.[29] These tests were performed in the laboratory of the Dalian Tuberculosis Prevention and Control Center which was evaluated as the national reference laboratory.

Statistical Analysis

We evaluated the epidemic trends associated with MDR-TB in Dalian in terms of initial drug resistance and acquired drug resistance for each anti-TB drug and across different age groups. Patients were divided into three age groups, based on age at the time of TB diagnosis: young (15–44 years), middle-aged (45–64 years), and older-aged (over 64 years). We did not include patients <15 years because only 6 patients were identified in this age group.

Descriptive statistics were employed to calculate the frequency (N) and percentage (%) of TB cases. The average annual growth rate (AAGR) was calculated as follows:

$$AAGR = \sqrt[Y]{\frac{\text{incidence in 2019}}{\text{incidence at baseline}}} - 1$$

where Y represents the number of years. Because the drugs of OFX and AMK were tested starting in 2013, their baseline was set to 2013 ($Y = 6$). All other drugs were tested based on the baseline of 2012 ($Y = 7$). MS Excel 2016 (Microsoft Corporation, Redmond, WA, USA) was used to establish the database and to generate graphs showing drug resistance trends. Statistical analyses were conducted using the SPSS 24.0 statistical package (IBM Corporation, Armonk, NY, USA). The Chi-square test was used to analyze the significance of variations in drug resistance trends during the study period. All tests of

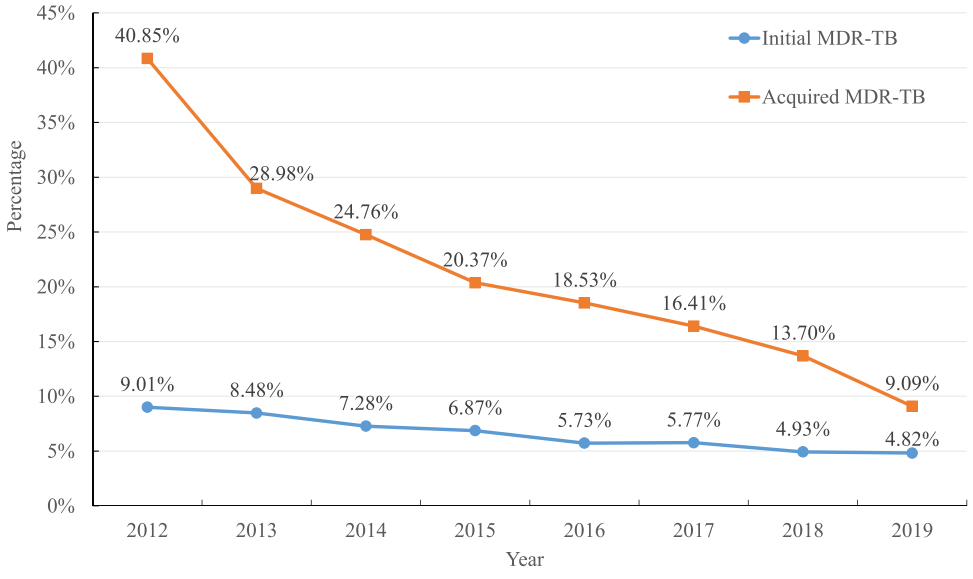

Figure 3 Prevalence of initial and acquired MDR-TB from 2012 to 2019 in Dalian.

significance were two-sided, and a *P-value* < 0.05 was considered significant.

Ethics Approval

The study was approved by the Ethics Committee of Dalian Tuberculosis Hospital, Dalian, China. Patient records were anonymized and de-identified prior to analysis, and we obtained permission from the dataset owner to use the information included in the database. This study was conducted in accordance with the Declaration of Helsinki.

Results

MDR-TB Prevalence from 2012 to 2019 in Dalian

The percentage of initial MDR-TB cases decreased from 9.01% in 2012 to 4.82% in 2019, with an average annual rate of decline of 8.55%, which represented a significant downtrend (χ^2 = 12.755, P < 0.001). The percentage of acquired MDR-TB cases decreased from 40.85% in 2012 to 9.09% in 2019, with an average annual rate of decline of 19.32%, which represented a significant downtrend (χ^2 = 66.382, P < 0.001, Figure 3).

Among previously treated cases, 70.59% (1248/1768) of patients were categorized as relapses, 7.13% (126/1768) of patients were categorized as initial treatment failure, and 22.29% (394/1768) were categorized as retreatment after initial treatment interruption. The MDR rates among relapsed patients were 34.78% in 2012, 24.81% in 2013, 17.73% in 2014, 15.68% in 2015, 18.81% in 2016, 12.03% in 2017, 11.26% in 2018, and 8.73% in 2019. Chi-square analysis revealed that the MDR rate among relapse patients exhibited a significant decline from 2012 to 2019 (χ^2 = 35.492, P < 0.001).

Initial and Acquired MDR-TB Prevalence Across Age Groups

Initial MDR-TB Prevalence in Different Age Groups

From 2012 to 2019, the initial MDR-TB rate among new young TB patients decreased from 13.33% to 4.51%, respectively, with an average annual rate of decline of 14.34%, representing a significant downtrend (χ^2 = 8.607, P = 0.003). The initial MDR-TB rate among new middle-aged TB patients decreased from 9.47% to 3.92%, with an average annual rate of decline of 11.84%, which represented a significant downtrend (χ^2 = 7.569, P = 0.006). However, no significant change in the MDR-TB rate was observed among new older-aged patients (P > 0.05, Figure 4).

Acquired MDR-TB Prevalence in Different Age Groups

From 2012 to 2019, the acquired MDR-TB rate among previously-treated young patients decreased from 46.59% to 11.76%, respectively, with an average annual rate of decline of 17.85%, representing a significant downtrend (χ^2 = 27.146, P < 0.001). The acquired MDR-TB rate among previously-treated middle-aged patients decreased from 34.15% to 8.97%, with an average annual rate of decline of 17.39%, which was a significant downtrend (χ^2 = 19.393,

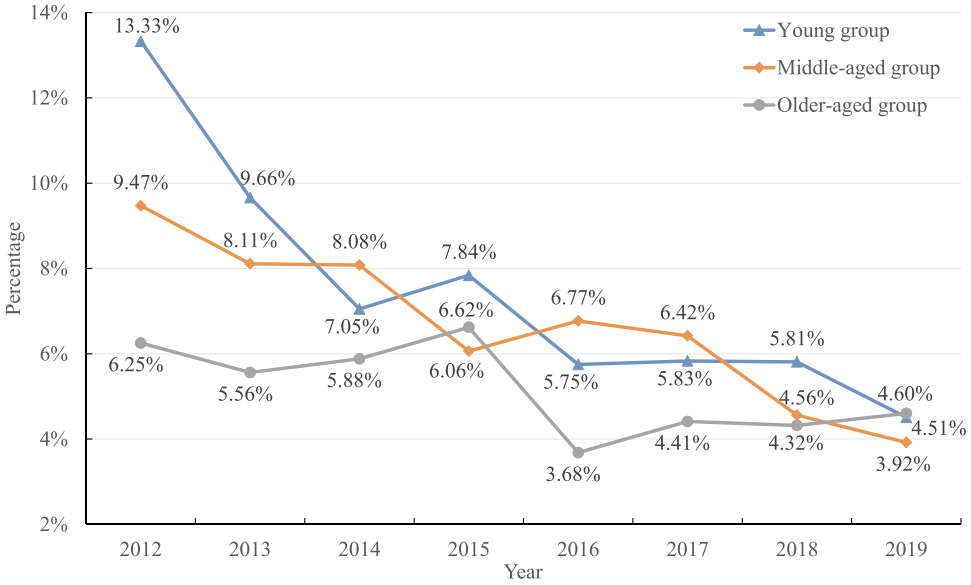

Figure 4 Prevalence of initial MDR-TB among different age groups from 2012 to 2019 in Dalian.

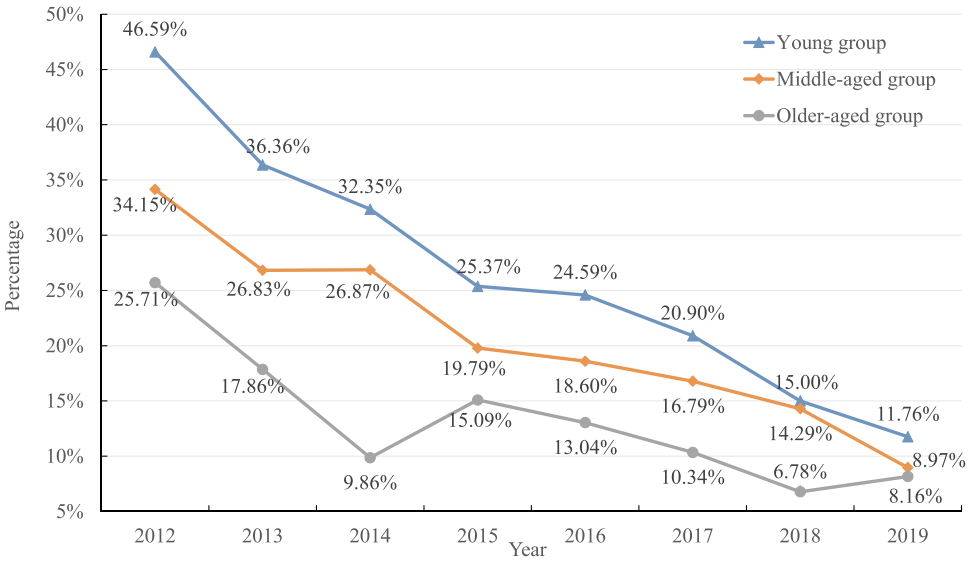

Figure 5 Prevalence of acquired MDR-TB among different age groups from 2012 to 2019 in Dalian.

$P < 0.001$). The acquired MDR-TB rate among previously-treated older-aged patients decreased from 25.71% to 8.16%, with an average annual decline rate of 15.12%, representing a significant downtrend ($\chi^2 = 5.817$, $P = 0.016$, Figure 5).

Specific Drug-Resistance Prevalence Among TB Patients

Specific Drug-Resistance Prevalence Among New TB Patients

From 2012 to 2019, the INH resistance rate among new TB patients decreased significantly, with an average annual rate of decline of 1.88%. The RFP resistance rate decreased from 14.59% to 7.31%, respectively, with an average annual rate of decline of 9.40%. The OFX resistance rate decreased from 6.87% in 2013 to 4.98% in 2019, with an average annual rate of decline of 5.22%. The AMK resistance rate decreased from 8.69% in 2013 to 1.19% in 2019, with an average annual rate of decline of 28.21%. All of these drug-resistance downtrends were significant ($P < 0.05$) using the Chi-square test for trends. However, the resistance rates for SM and EMB exhibited no significant changes ($P > 0.05$, Table 1).

Specific Drug-Resistance Prevalence Among Previously Treated TB Patients

From 2012 to 2019, among previously treated TB patients, the INH resistance rate decreased from 44.51% to 21.82%, with an average annual rate of decline of 9.68%. The RFP resistance rate decreased from 52.44% to 15.15%, with an average annual rate of decline of 16.25%. From 2013 to 2019, among previously treated TB patients, the OFX resistance rate decreased from 18.18% to 8.48%, with an average annual rate of decline of 11.94%. The AMK resistance rate decreased from 11.93% to 1.21%, with an average annual rate of decline of 31.71%. All of these drug-resistance downtrends were significant ($P < 0.001$) using the Chi-square test for trends. However, the downtrends observed for SM and EMB resistance were not significant ($P > 0.05$, Table 2).

Discussion

The initial drug-resistance rate, especially the initial multi-drug-resistance rate, could serve as an important indicator for evaluating the efficacy of prevention and control strategies applied to MDR-TB.[18,19] The present study found that the initial drug resistance rate decreased significantly, by almost half, between 2012 and 2019. This decreasing trend may be due to multiple interventions that were implemented in this region. First, the WHO-endorsed GeneXpert was widely used in this region, allowing for the rapid diagnosis of MDR-/RR-TB cases compared with the speed of conventional phenotypic methods.[30] Second, all identified MDR-TB patients were hospitalized until bacterial conversion was verified by smear microscopy. Significant reductions in the bacterial load of sputum samples can reduce the transmission of MDR-TB in the community. Third, FDC drugs were widely used, which could effectively prevent the emergence of new MDR-TB strains.[31,32] Therefore, promoting the widespread usage of FDC drugs appears to be an effective measure for

Table 1 Drug Resistance Trends for INH, RFP, EMB, SM, OFX, and AMK in New TB Patients in Dalian from 2013 to 2018

Year	N	INH (n, %)	RFP (n, %)	SM (n, %)	EMB (n, %)	OFX (n, %)	AMK (n, %)
2012	233	24(10.30)	34(14.59)	22(9.44)	8(3.43)	–	–
2013	495	68(13.74)	74(14.95)	50(10.10)	6(1.21)	34(6.87)	43(8.69)
2014	714	117(16.39)	76(10.64)	70(9.80)	13(1.82)	57(7.98)	43(6.02)
2015	655	87(13.28)	64(9.77)	69(10.53)	10(1.53)	42(6.41)	18(2.75)
2016	628	70(11.15)	69(10.99)	69(10.99)	18(2.87)	33(5.25)	16(2.55)
2017	624	77(12.34)	70(11.22)	61(9.78)	18(2.88)	48(7.69)	10(1.60)
2018	719	61(8.48)	45(6.26)	59(8.21)	12(1.67)	28(3.89)	11(1.53)
2019	643	58(9.02)	47(7.31)	69(10.73)	16(2.49)	32(4.98)	8(1.19)
Chi-square		15.949	25.605	0.057	0.506	7.114	65.924
P-value		< 0.001	< 0.001	0.812	0.477	0.008	< 0.001

Note: The OFX and AMK were not tested in 2012.
Abbreviations: INH, isoniazid; RFP, rifampicin; SM, streptomycin; EMB, ethambutol; OFX, ofloxacin; AMK, amikacin.

Table 2 Drug Resistance Trends for INH, RFP, EMB, SM, OFX, and AMK in Previously Treated TB Patients in Dalian from 2013 to 2018

Year	N	INH (n, %)	RFP (n, %)	SM (n, %)	EMB (n, %)	OFX (n, %)	AMK (n, %)
2012	164	73(44.51)	86(52.44)	24(14.63)	20(12.20)	–	–
2013	176	67(38.07)	75(42.61)	20(11.36)	8(4.55)	32(18.18)	21(11.93)
2014	307	108(35.18)	102(33.22)	54(17.59)	24(7.82)	65(21.17)	19(6.19)
2015	216	50(23.15)	63(29.17)	32(14.81)	12(5.56)	15(6.94)	11(5.09)
2016	259	73(28.19)	77(29.73)	43(16.60)	13(5.02)	35(13.51)	8(3.09)
2017	262	67(25.57)	77(29.39)	37(14.12)	31(11.83)	32(12.21)	6(2.29)
2018	228	39(17.11)	56(24.56)	19(8.33)	11(4.82)	17(7.46)	5(2.19)
2019	165	36(21.82)	25(15.15)	24(14.55)	11(6.67)	14(8.48)	2(1.21)
Chi-square		46.218	59.264	1.258	0.698	20.257	28.816
P-value		< 0.001	< 0.001	0.262	0.403	< 0.001	< 0.001

Note: The OFX and AMK were not tested in 2012.
Abbreviations: INH, isoniazid; RFP, rifampicin; SM, streptomycin; EMB, ethambutol; OFX, ofloxacin; AMK, amikacin.

reducing acquired drug resistance, which likely has an indirect effect on the rate of initial drug resistance.

Unlike initial drug-resistant TB, the spectrum of acquired drug-resistant TB patients reflects previously treated cases; therefore, this population does not provide a good measure of the efficacy of recently implemented control strategies.[7] However, our study showed that the acquired MDR-TB rate showed a significant decreasing trend, similar to that observed for the initial MDR-TB rate ($P < 0.001$). Although this decrease in the acquired MDR-TB rate was likely associated with improvements in treatment and management strategies, we speculate that the implementation of nosocomial infection control strategies might represent another critical determinant of acquired MDR-TB reduction.

Before MDR isolation wards were established, MDR-TB and drug-sensitive TB patients were maintained in the same ward, which increased the risk of transmitting MDR strains to drug-sensitive TB patients during treatment and increased indirectly the risk of treatment failure.

Independent drug-resistance wards were established starting in 2012 in Dalian, which coincided with a significant decline in the acquired drug-resistance rate, from 40.85% in 2012 to 28.98% in 2013, providing indirect evidence for our hypothesis.[33] In a recent population-based study by Shen et al, relapse cases in China were found to be more strongly associated with exogenous infections rather than endogenous recurrence.[34] Unfortunately, the present study did not sequence the genomes of the MDR-TB strains, and no molecular epidemiological evidence was collected that could be used to determine whether infection control strategies had effects on the decline in acquired drug-resistance rates.

This study found that both initial and acquired MDR-TB was more prevalent in the young group than in either the middle-aged or older-aged groups. In 2012, young patients (46.59%) with a previous treatment history had the highest rate of MDR-TB compared with middle-aged (34.15%) and older-aged patients (25.71%), which suggested serious challenges to MDR-TB control at that time. More middle-aged and older-aged MDR-TB patients were previously treated cases, which were associated with accumulating tends and these were more likely to reflect the past MDR-TB prevalence, whereas the young group was more likely to represent newly infected MDR cases, which presented the latest MDR-TB prevalence. Therefore, we speculate that the significant downtrend observed in the prevalence of young MDR-TB rates in 2013 was associated with improved control of nosocomial infections.

We further evaluated trends in the initial and acquired MDR-TB rates across different age groups and identified significant downtrends in the rates observed for the young ($P < 0.05$) and middle-aged groups ($P < 0.05$); however, the initial and acquired MDR-TB rates among the older-aged group appeared to be low and stable, especially for initial MDR-TB patients ($P > 0.05$). Based on the hypothesis of exogenous infection, we speculate that this difference may reflect the societal roles of younger and middle-aged individuals, who represent the main labor force and have great social mobility, whereas older-aged individuals were engaged in relatively limited activity,[24,35,36] and less migration, resulting in this population being less likely to be at risk of exogenous infections.[37]

Notably, the resistance rates to most of the drugs tested in this study also decreased significantly from 2012 to 2019 ($P < 0.05$), including RIF, INH, OFX, and AMK. In contrast, no significant declines in the drug-resistance rates were observed for EMB and SM ($P > 0.05$). On the one hand, SM is rarely used due to high levels of drug resistance and side effects; therefore, the drug resistance levels are likely to reflect the drug resistance of TB older strains.[38] On the other hand, compared with other anti-TB drugs, distinguishing between susceptible and resistant isolates may be difficult when testing EMB and SM using in vitro DST.[39] As a consequence, the DST results for these two drugs may be less reliable than those for other drugs, which may explain the pattern of drug-resistant rates observed for these two drugs across the study period.[40,41]

Several limitations should be mentioned for this study. First, the large sample and retrospective study design introduced an increased possibility that errors may have been introduced during case registration or the recording of drug-resistance surveillance results. Second, limited by MDR-TB sample size, the population could only be divided into three age groups: young (15–44 years), middle-aged (45–64 years), and older-aged (over 64 years) to analyze MDR-TB trends. The young group covered more age range in the present study, which may result in trouble for a reasonable interpretation of the results. Third, when analyzing previously treated TB patients, we chose patients with relapse, initial treatment failure, and retreatment after treatment interruption, but other categories (eg, irregular medication for more than one month) were excluded, which could underestimate the epidemic trend of previously treated MDR-TB. Finally, we speculated that the implemented prevention and treatment strategies that were designed to reduce the transmission of TB played an important role in MDR-TB control; however, we did not obtain genotyping data and or molecular epidemiological data that could support this speculation.

Conclusion

Although the total treatment success rate of MDR-TB up to 62.6% from 2012 to 2019 in Dalian, which is higher than the global average, the decline in the MDR-TB epidemic should not be attributed solely to medical treatment. More attention should be paid to the implementation of multiple measures for prevention and control, including controlling the MDR-TB infection among the community and preventing non-drug-resistant TB patients from deteriorating into MDR-TB patients. The MDR-TB epidemic may be reversed in the short term by interrupting the community and nosocomial transmission of MDR-TB strains and preventing the emergence of new MDR-TB strains through the application of standardized treatment regimens. This study indicates

some effective strategies that can be implemented by developing countries with relatively scarce economic resources to control the prevalence of MDR-TB.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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