

Recent Transmission and Prevalent Characterization of the Beijing Family *Mycobacterium tuberculosis* in Jiangxi, China

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Abstract

The Beijing genotype is the most common type of tuberculosis in Jiangxi Province, China. The association of population characteristics and their prevalence in the development of recent transmission is still unclear. 1,433 isolates were subjected to drug-resistance tests and MIRU-VNTR analysis. We compared differences in demographic characteristics and drug resistance patterns between the Beijing and non-Beijing family strains. We also explored the association of the clustering rate with the Beijing genotype of *Mycobacterium tuberculosis*. The Beijing genotype was dominant (78.16%). The results of MIRU-VNTR showed that 775 of 1,433 strains have unique patterns, and the remaining gather into 103 clusters. A recent transmission rate was 31.54% (452/1,433). The Beijing genotype strains were more likely to spread among

the recurrent population ($p=0.004$), people less than 50 years of age ($p=0.02$ or 0.003), and the personnel in the northern regions ($p=0.03$). Drug resistance patterns did not show significant differences between Beijing and non-Beijing genotype isolates. Furthermore, we found that HIV-positive cases had a lower clustering rate ($p=0.001$). Our results indicated that the recurrent population and people under 50 years of age were more likely to be infected with the Beijing genotype of *M. tuberculosis*. The strains from the Beijing family were easier to cluster compared to strains isolated from the non-Beijing family. Social activity and AIDS substantially impacted the clustering rate of the Beijing genotype of *M. tuberculosis*. Multidrug resistant *M. tuberculosis* affected Beijing genotype transmission.

Key words: *Mycobacterium tuberculosis*, Beijing genotype, prevalent characterization, clustering

Introduction

Tuberculosis (TB) remains a health threat to humans. According to the World Health Organization (WHO) 2020 Global tuberculosis report (WHO 2020), there were 10.0 million new cases of TB and 1.5 million deaths from TB in 2019. China has the second largest number of patients with TB, multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB), or extensively multidrug-resistant *M. tuberculosis* (XDR-TB), only behind India (WHO 2020). MDR-TB shows resistance to at least isoniazid and rifampin. XDR-TB exhibits additional resistance to all kinds of fluoroquinolone and a second-line injectable drug. Although aggressive TB control has resulted in a sharp decrease in cases

in recent years, it remains a public health concern in China. In Jiangxi, a southeast province of China, the prevalence of TB is also high. According to the Chinese national baseline surveillance, the prevalence of tuberculosis in Jiangxi province was 230/100,000 in 2010. Therefore, there is an urgent need to reduce the prevalence of tuberculosis. Considering that the main epidemic tuberculosis strains were Beijing genotype strains in Jiangxi Province, it is necessary to investigate the infection status, epidemiological characteristics, and risk factors of Beijing genotype strains (Luo et al. 2019).

Molecular typing technologies have been used to determine the genotypic diversity of *M. tuberculosis* (MTB), which played an important role in TB control

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and understanding of recent transmission. Mycobacterial Interspersed Repetitive Units and Variable Number of Tandem Repeats (MIRU-VNTR) is a powerful tool to differentiate the *M. tuberculosis* complex into various clusters and define the recent transmission. As the most evolved biological lineage among seven human-adapted phylogenetic lineages, the Beijing lineage strains show a global distribution. According to the statistics, more than 50% of these strains were present in East and South East Asia (Brudey et al. 2006). It is very valuable to have a broad knowledge of the association of the characteristics of the Beijing genotype *M. tuberculosis* with social demography. One study (Singh et al. 2015) suggested that drug resistance was related to its genotype, which appeared quickly in Beijing genotype strains (Maeda et al. 2014). Some studies even considered that age, gender, and region have important effects on the recent transmission of Beijing family strains (Yang et al. 2012; Zanini et al. 2014; Mohajeri et al. 2016).

Jiangxi is facing the health challenge of TB prevention and control (Chen et al. 2019; Luo et al. 2019). However, the association between the prevalence of Beijing genotype strains and the related characterization is still unclear. To understand whether there is an association between Beijing genotype strains and patient characterization, we investigated sociodemographic factors and drug susceptibility tests (DST) between Beijing genotype and non-Beijing genotype strains in Jiangxi province.

Experimental

Materials and Methods

***Mycobacterium tuberculosis* isolates.** All data were obtained from the Jiangxi Chest Hospital from January to December 2016. TB patients came from all places in Jiangxi province, and all patients with lung TB were included in this period. Three sputum samples from patients suspected of pulmonary TB were collected for the Ziehl-Neelsen staining and cultured in Löwenstein-Jensen and MGIT 960 media. Conventional chemical methods, such as thiophene carboxylic acid hydrazide and p-nitrobenzoic acid, were used to differentiate the *M. tuberculosis* complex (MTBC) from non-tuberculous mycobacteria (NTM). The study was approved by the Ethics Committee of The First Affiliated Hospital of Nanchang University and the Institutional Review Board of The Jiangxi Chest Hospital. Written informed consent was obtained from all patients. All methods adhered to the relevant guidelines and regulations in China.

Drug susceptibility tests. The tests for all MBT isolates were performed using BACTEC MGIT 960 (Becton, Dickinson and Company, USA) (Iseman and

Heifets 2006). These drugs included isoniazid (INH), rifampin (RIF), streptomycin (SM), ethambutol (EMB), levofloxacin (LEV), amikacin (AMK) (1.0 µg/ml), and capreomycin (CM). Negative quality control was performed routinely using H37Rv. The results were interpreted according to the MGIT 960 operating manual (Ma et al. 2018).

Data collection and definitions. We collect demographic, epidemiological, and clinical data from TB patients. The term 'recurrent' patients met previously reported criteria in the literature (Zong et al. 2018), and habitat referred to the area where the household registration was located. In this study, the 'cluster' was defined as two patients whose isolates had the same MIRU-VNTR patterns. The percentage of recent transmission, which was our primary outcome measure, was calculated using the formula: $(NC - C)/N$, where NC is the total number of isolates, C is the number of groups, and N is the total number of groups.

Genotyping methods. Genomic DNA was obtained by boiling lysis. Following the previously described protocol (Chen et al. 2016), amplification of MIRU-VNTR 15 locus was performed to analyze the genotype of these strains. Briefly, MIRU-VNTR loci were first amplified by PCR. The PCR products were then examined by electrophoresis with 1.5% agarose gels. The size of the PCR fragments was visualized using the Gel Image Analysis System (LiuYi Co., China). The repeat numbers of various MIRU-VNTR loci were calculated by comparing them with H37Rv. The RD105 DTM-PCR method was used to determine whether the strain belongs to the Beijing strain or not (Chen et al. 2007).

Data management and analysis. Using BioNumerics 6.6, we analyzed the bacterial genotyping and visualized the evolutionary relationships between these clinical isolates. The MIRU-VNTR results were used to construct a dendrogram based on the UPGMA algorithm. A 'cluster' was defined as a group of two or more patients who shared the same 15-locus MIRU-VNTR profile. The discrimination of the locus combination was calculated using the Hunter-Gaston discriminatory index (HGDI) (Hunter and Gaston 1988):

$$HGI = 1 - \frac{1}{N(N-1)} \sum_{j=1}^s n_j(n_j-1) \quad (1)$$

where N is the total number of TB isolates, s is the number of distinct patterns discriminated by MIRU-VNTR, and n_j is the number of isolates belonging to the jth pattern. Allelic diversity (h) was done using the equation:

$$h = 1 - \sum x_i^2 \left(\frac{n}{n-1} \right) \quad (2)$$

where n is the number of isolates and x_i is the frequency of the i-th allele at the locus (Selander et al. 1986). As

previously reported, the clustering rate was defined as (ncc)/n as (Small et al. 1994). Between patients infected with the Beijing genotype and non-Beijing genotype strains, the distribution of genotype, sex, age, treatment history, region, clinical specimen types, and DST profile was assessed using the chi-square test SPSS17.0 (SPSS Inc., USA). $p < 0.05$ was considered statistically significant.

Results

The most popular MTB family was the Beijing genotype. In total, 8,351 suspected pulmonary TB patients visited Jiangxi Chest Hospital from January

to December 2016, and 20.91% (1,746/8,351) were cultured positive. After excluding 96 non-tuberculous mycobacteria (NTM) and 217 contaminated MTB, 1,433 strains were adopted. Of all, 658 strains were clustered, and 775 were unique isolates. 1,220 MTB belonged to the Beijing family, including 612 strains that clustered and 508 had unique patterns. Compared to strains from the non-Beijing family, isolates from the Beijing family clustered more easily ($p = 0.001$, OR (95% CI): 6.99 (5.01–9.77)). All results are shown in Fig. 1.

Distribution of isolates. A total of 1,433 strains were acquired from patients diagnosed with tuberculosis during this period in Jiangxi province, China. Of all 1,433 isolates, 376 (26.24%, 376/1,433) were from Nanchang, 246 (17.17%, 246/1,433) from Shangrao,

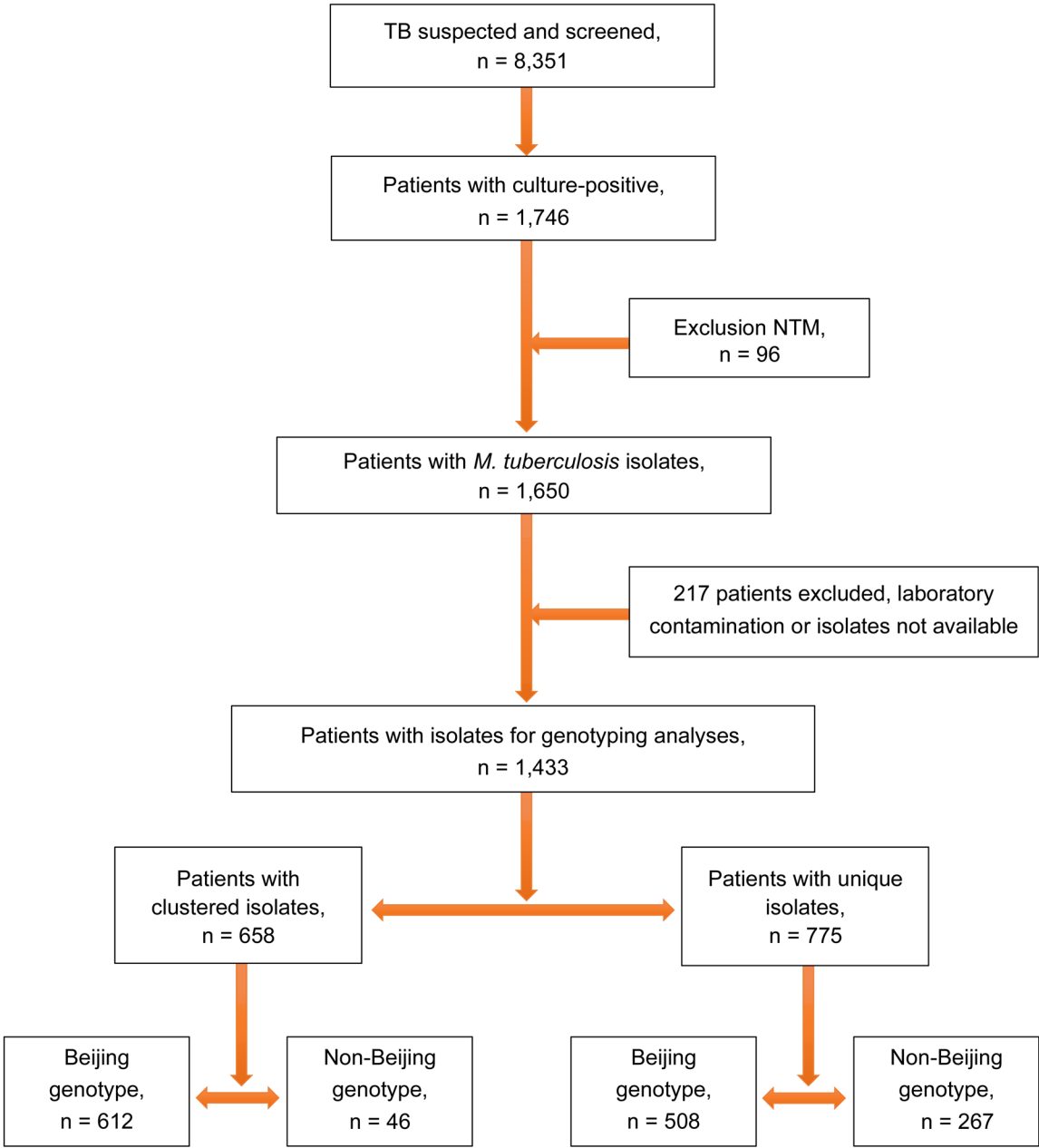


Fig. 1. The MIRU-VNTR genotypes in Jiangxi province, China – the study design. NTM – nontuberculous mycobacteria.

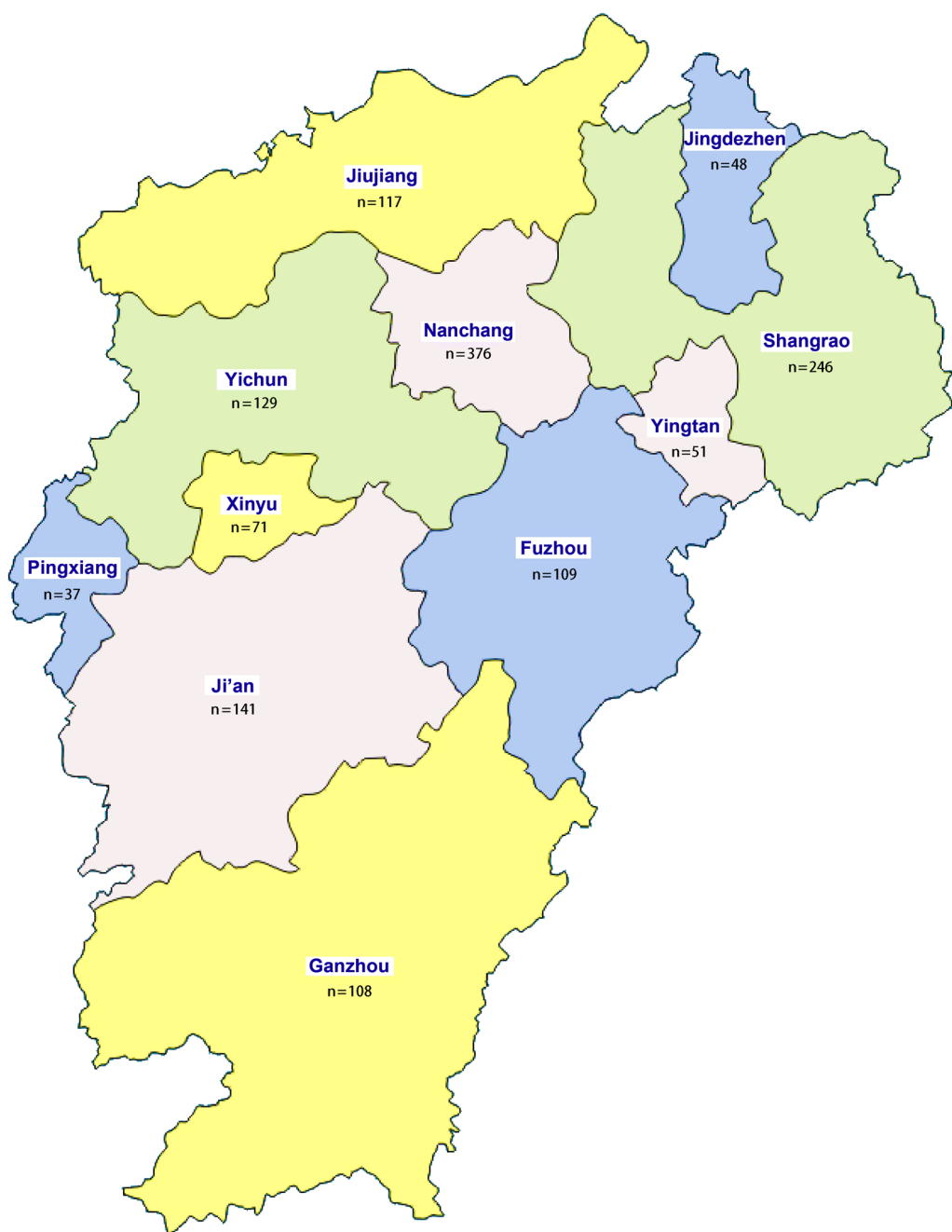


Fig. 2. Map of Jiangxi showing the distribution of 1,433 isolates included in this study (the numbers indicate the absolute number of isolates in every region).

141 (9.84%, 141/1,433) from Ji'an, 129 (9.00%, 129/1,433) from Yichun, 117 (8.16%, 117/1,433) from Jiujiang, 109 (7.61%, 109/1,433) from Fuzhou, 108 (7.54%, 108/1,433) from Ganzhou and 207 (14.44%, 207/1,433) from other districts. Consequently, for 1,120 strains of the Beijing family, 282 (282/1,120) of them were from Nanchang, 199 (199/1,120) from Shangrao, 118 (118/1,120) from Ji'an, 103 (103/1,120) from Yichun, 84 (84/1,120) from Jiujiang, 90 (90/1,120) from Fuzhou, 91 (91/1,120) from Ganzhou, and 153 (153/1,120) from the rest districts (Fig. 2, Table SI). According to the Jiangxi regional distribution, the whole province can be divided into three regions, including southern regions

(Ganzhou and Ji'an districts), central regions (Nanchang, Fuzhou, Yichun, Xinyu, and Pingxiang districts), and northern regions (Jiujiang, Jingdezhen, Shangrao and Yingtan districts). Among 1,433 isolates, the majority come from the central regions (722, 50.38%), followed by the northern regions (462, 32.24%) and the southern regions (249, 17.38%). Fig. 2 indicates the different geographical sources of these isolates.

Demographic characteristics and drug resistance patterns. Table I shows the demographic characteristics of these patients. Among 1,433 patients, 860 were men, and 573 were women. Age ranged from 3 to 89 years, with an average age of 43.61. Regarding the history of

Table I
Demographic and drug-resistant characteristics of this study's isolates (n = 1,433).

Characteristics	Number	Beijing family	Non-Beijing family	OR (95% CI)	p-value
All	1,433	1,120	313	–	–
Sex					
Men	860	651	209	–	–
Women	573	419	154	1.14 0.90–1.46	0.29
Age					
≥ 50	512	376	136	–	–
30–50	467	381	86	1.44 1.14–1.83	0.003
≤ 30	454	363	91	1.33 1.05–1.67	0.02
Treatment history					
New	1,174	900	274	–	–
Recurrent	168	145	23	0.52 0.33–0.83	0.004
Treatment failure	91	75	16	0.70 0.40–1.22	0.24
Region					
Southern regions	249	181	68	–	–
Central regions	722	567	155	0.73 0.52–1.01	0.07
Northern regions	462	372	90	0.64 0.45–0.92	0.02
DST profile					
DST profile	1,433	1,120	313	–	–
Pansusceptible	992	794	198	0.89 0.73–1.09	0.27
RIF	27	18	9	1.79 0.80–4.02	0.16
INH	33	25	8	1.14 0.51–2.56	0.68
SM	52	44	8	0.65 0.30–1.40	0.31
EMB	6	5	1	0.72 0.08–6.15	1.00
AK	19	15	4	0.95 0.31–2.90	1.00
CM	18	13	5	1.38 0.49–3.89	0.57
LEV	38	30	8	0.95 0.43–2.10	1.00
RIF + INH	56	47	9	0.68 0.33–1.41	0.41
RIF + SM	20	15	5	1.19 0.43–3.31	0.78
INH + SM	41	34	7	0.74 0.32–1.68	0.57
RIF + EMB	5	3	2	2.39 0.40–14.34	0.30
INH + EMB	1	1	0	–	–
RIF + INH + EMB	71	60	11	0.66 0.34–1.26	0.24
RIF + INH + SM	29	25	4	0.57 0.20–1.66	0.37
INH + SM + EMB	5	4	1	0.90 0.10–8.03	1.00
RIF + INH + SM + EMB	2	1	1	3.58 0.22–57.37	0.39
MDR	158	133	25	0.64 0.41–1.01	0.05

treatment, 1,174 patients received single treatment, and 257 patients were treated at least twice (including 168 recurrent cases and 91 treatment failure cases). There was a total of 1,120 (1,120/1,433, 78.16%) MTB belonging to the Beijing family. Compared to cases of *M. tuberculosis* of the non-Beijing lineage, we found a significant difference in the Beijing family isolates among young and middle-aged people (less than 50 years old), people with recurrent status, and personnel in the northern regions. More than half of the patients (722, 50.38%) came from the central regions. Among them, 992 isolates (992/1,433, 69.22%) were sensitive to the four first- and three second-line antituberculosis drugs, and 441 isolates (441/1,433, 30.78%) were resistant to at least one of these drugs. A total of 29.11% (326/1,120) of drug-resistant tuberculosis belonged to the Beijing genotype, and that of MDR-TB was 40.80% (133/326). The drug-resistant rate of RIF/INH/SM/EMB/AK/LEV/CM in the Beijing genotype family strains (15.09%/17.23%/10.62%/6.25%/1.34%/2.68%, respectively) was higher than that in non-Beijing strains (13.10%/12.78%/7.99%/4.79%/1.28%/2.56%, respectively). However, statistical analysis did not reveal such a statistical difference. We also compared the percentage of strains resistant to multidrug (two or more drugs) resistant strains between the Beijing and non-Beijing genotype strains. The only difference was found in MDR-TB (11.88% vs. 7.35%, $p=0.05$, OR (95% CI): 0.64 (0.41–1.01)) (Table I).

Genotypes of *M. tuberculosis* strains. To investigate the genotypes of 1,433 *M. tuberculosis*, the MIRU-VNTR method was adopted. Of these strains, 78.2% (1,120/1,433) belonged to the Beijing genotype strains, and the rest were non-Beijing genotype strains (Table SII). Non-Beijing genotype families, including the S, Cameroon, and NEW-1 families, adopted the strain identification method (<https://www.miru-vntrplus.org/MIRU/index.faces>).

To investigate the allelic diversity of these MIRU-VNTR loci, we calculated the Hunter-Gaston discriminatory index (HGDI) for each locus. As previously reported, the MIRU-VNTR loci were considered highly discriminatory (>0.6), moderately (0.3–0.6), or poorly (<0.3) discriminatory loci based on HGDI scores (Chen et al. 2016). These loci had a significant discriminatory ability with various HGDI scores (Table SII). According to the situation described above, three loci were considered highly discriminatory, including MIRU26 (HGDI = 0.6580), Qub26 (HGDI = 0.6344), and ETRE (HGDI = 0.6320). Eight loci (Mtub04, MIRU40, MIRU10, Mtub21, Qub11b, Mtub30, Mtub39, and Qub4156) had a moderate discriminatory ability, and the biomarkers of the remains were poorly discriminatory loci. The 15-loci discriminatory power reached 0.9963. At the same time, 1,433 strains were classified

into 878 genotypes by adopting MIRU-VNTR cluster analysis, including 103 clusters and 775 unique patterns. The largest cluster was made up of 67 strains, and 11 clusters were made up of two strains. As a result, the clustering rate was 38.7% (555/1,433), and the recent transmission rate was 31.5% (452/1,433).

Association with the recent transmission of Beijing genotype strains. To understand whether prevalent characteristics impact Beijing lineage tuberculosis's clustering ability and composition, we performed a statistical analysis to reveal the relationship between clustering ability and Beijing family bacteria. The information is shown in Tables II and III. The results showed that the non-clustered bacteria showed a stronger tendency to infect women (non-Beijing family strains, $p=0.03$, OR (95% CI): 1.50 (1.06–2.14); Beijing family strains, $p=0.001$, OR (95% CI): 1.52 (1.20–1.93)). Furthermore, when the Beijing family bacteria infected people, patients between 30 and 50 years of age were more likely to be clustered ($p=0.003$, OR (95% CI): 3.02 (1.53 to 5.97)) compared to those less than 30 years of age. Among patients who do not cluster, the amount of bacteria from the Beijing family is significantly higher than the Beijing family bacteria ($p=0.012$, OR (95% CI): 0.68 (0.51–0.91)). Regarding treatment history, the recurrent infection of Beijing family bacteria is more often clustered ($p=0.05$, OR (95% CI): 0.65 (0.43–0.99)). Meanwhile, among patients infected with clustered bacteria, the Beijing family is significantly different from non-Beijing family bacteria in recurrence and treatment failure cases (Table III). To understand the role of AIDS, sputum smear, and lung cavity in the transmission of Beijing family strains, we compared HIV-negative, sputum smear-negative, and non-pulmonary cavity patients with the corresponding positive ones. We identified that the clustering rate between HIV-positive cases was significantly lower than that of non-clustered positive cases ($p=0.001$, OR (95% CI): 0.20 (0.09–0.45)), while the smear-negative non-clustered Beijing family bacteria negative to smears was significantly lower than that of smear-positive bacteria of non-Beijing family ($p=0.001$, OR (95% CI): 0.57 (0.41–0.80)). However, the pulmonary cavity did not affect the clustering of *M. tuberculosis* and the composition of the Beijing genotype.

Discussion

To better implement preventive measures in Jiangxi province, it is necessary to understand the association of Beijing genotype *M. tuberculosis* transmission and its prevalent characterization. Beijing genotype *M. tuberculosis* was considered one of the most successful lineages, and it was more transmissible than other families

Table II
Prevalent characterization of clustered and non-clustered strains.

Characteristics	Clustered				Non-clustered			
	Beijing family n = 612	Non-Beijing family n = 46	OR (95%CI)	p-value	Beijing family n = 508	Non-Beijing family n = 267	OR (95%CI)	p-value
Sex								
Men	384	32	–	–	267	177	–	–
Women	228	14	0.74 0.38–1.41	0.43	241	90	0.56 0.41–0.77	< 0.001
Age								
≤ 30	187	13	–	–	176	78	–	–
30–50	232	19	1.18 0.57–2.45	0.72	149	67	1.02 0.68–1.50	1.00
≥ 50	193	14	1.04 0.48–2.28	1.00	183	122	1.504 1.06–2.14	0.03
Treatment history								
New	507	28	–	–	443	246	–	–
Recurrent	84	14	3.02 1.53–5.97	0.003	61	9	0.266 0.13–0.54	0.00
Treatment failure	21	4	3.449 1.11–10.73	0.05	4	12	5.402 1.72–16.93	0.002
HIV status								
Negative	584	37	–	–	485	260	–	–
Positive	28	9	0.20 0.09–0.45	0.001	23	7	1.76 0.75–4.16	0.24
Sputum								
Negative	121	12	–	–	104	83	–	–
Positive	391	34	0.88 0.44–1.75	0.72	404	184	0.57 0.41–0.80	0.001
Cavity								
Yes	108	7	–	–	86	42	–	–
No	504	39	1.19 0.52–2.74	0.84	422	225	1.09 0.73–1.63	0.76

of *M. tuberculosis* in Peru children (Huang et al. 2020). To understand TB's characteristics and seek methods to prevent a local TB epidemic, it is necessary to know the molecular prevalence of *M. tuberculosis* (Song et al. 2020). In this study, we collected 1,433 TB isolates and tried understanding the detailed population status between Beijing and non-Beijing family isolates. We also investigated the association of the prevalence of the Beijing *M. tuberculosis* genotype with normal characterization and drug resistance. The aim was to reveal the association between clustered ability and different MTB features in Jiangxi province. We found that men were more likely to be infected with tuberculosis, which is consistent with the reported literature (Liu et al. 2018), while some references have a converse viewpoint (Hertz and Schneider 2019; Yang et al. 2021). The reason might be attributed to geographical differences. We also found that women were more likely to be infected by non-clustered strains (Tables II and III). The reason might

be that the women had fewer social activities and less interpersonal contact, leading to less exposure to TB patients (Lin et al 2021). In addition to gender, age was another important factor for Beijing genotype strain infection. Two previous studies showed that younger people (less than 25 years old) were prone to be infected with Beijing genotype strains (Pang et al. 2012; Huang et al. 2020). Our analysis also had the same results that young people (less than 30 years old) were more likely to be infected with the Beijing genotype *M. tuberculosis* compared to older adults (more than 50 years old) (Table I). Furthermore, we found that middle-aged people (30–50 years old) infected with Beijing family bacteria were more likely to cluster compared to those less than 30 years old (Table IV) (Mathema et al. 2017). Moreover, we also found that the population in northern regions was more easily infected by Beijing family bacteria, probably because the north of Jiangxi is closer to the north

Table III
Prevalent characterization of Beijing and non-Beijing family strains.

Characteristics	Beijing family				Non-Beijing family			
	Clustered n = 612	Non- clustered n = 508	OR (95% CI)	<i>p</i> -value	Clustered n = 46	Non- clustered n = 267	OR (95% CI)	<i>p</i> -value
Sex								
Men	384	267	–	–	32	177	–	–
Women	228	241	1.52 1.20–1.93	0.001	14	90	1.16 0.59–2.29	0.74
Age								
≤30	187	176	–	–	13	78	–	–
30–50	232	149	0.68 0.51–0.91	0.01	19	67	0.588 0.27–1.28	0.24
≥50	193	183	1.01 0.76–1.34	1.00	14	122	1.45 0.65–3.25	0.41
Treatment history								
New	530	461	–	–	32	203	–	–
Recurrent	67	38	0.65 0.43–0.99	0.05	11	52	0.74 0.35–1.58	0.42
Treatment failure	15	9	0.69 0.30–1.59	0.42	3	14	0.74 0.20–2.70	0.71
HIV status								
Positive	28	23	–	–	2	14	–	–
Negative	584	485	1.01 0.58–1.78	1.00	44	253	0.82 0.18–3.74	1.00
Sputum								
Negative	121	104	–	–	12	83	–	–
Positive	391	404	1.20 0.89–1.62	0.23	34	184	0.78 0.39–1.59	0.60
Cavity								
No	494	432	–	–	39	225	–	–
Yes	118	76	1.36 0.99–1.86	0.07	7	42	0.96 0.40–2.30	1.00

of China, where there are more Beijing family strains (Chen et al. 2018). At the same time, we found that the recurrent population was more easily infected by the Beijing genotype *M. tuberculosis*, which could be carried for an extended period and spread easily. Molecular epidemiology has increased our understanding of the prevalence of tuberculosis.

We found that the Beijing genotype was significantly associated with clustering, suggesting that recent transmission was substantially different from non-Beijing genotype strains, consistent with a study of Shanghai (Zanini et al. 2014).

Evidence has shown that the drug-resistance ability of *M. tuberculosis* has no correlation with sublineages (Yuan et al. 2015). Our results also proved no association between drug-resistant patterns and the Beijing genotype. However, Beijing genotype strains are more likely to develop MDR-TB, consistent with the previous report (Zhou et al. 2017). AIDS is a significant risk fac-

tor for TB infection (Bell and Noursadeghi 2018; Khan et al. 2019). Our study found that the HIV-positive population had a lower clustering rate. We deduce that this is because patients with AIDS are more prone to endogenous recurrence due to low immune function (Jasenosky et al. 2015; Amelio et al. 2019).

Although we have demonstrated important findings, this study has some limitations. Firstly, we use traditional MIRU-VNTR methods to study all TB transmission, while some patients with the same MIRU-VNTR patterns did not have epidemiological links. As a result, recent transmission rates were overestimated (Chen et al. 2016). MIRU-VNTR is more convenient and cost-effective than whole-genome sequencing (WGS); it is also of great value in defining the recent transmission of tuberculosis (Rizvi et al. 2020). Second, concerns about risk factors for defining clusters and distinguishing Beijing genotype were arguable. We had no opportunity to overcome selection bias for incomplete

data on tuberculosis in the local population. However, the individuals in our study were completely random. Therefore, our findings had a high level of feasibility. In conclusion, our results had a specific value in controlling tuberculosis spread, especially for the Beijing genotype *M. tuberculosis*.

Abbreviations

MTB	– <i>Mycobacterium tuberculosis</i>
DST	– drug susceptibility testing
MIRU-VNTR	– mycobacterial interspersed repetitive units and variable number of tandem repeats
MDR-TB	– multidrug-resistant tuberculosis
RR-TB	– rifampicin-resistant TB
MTBC	– <i>M. tuberculosis</i> complex
NTM	– nontuberculosis mycobacteria
INH	– isoniazid
RIF	– rifampin
SM	– streptomycin
EMB	– ethambutol
LEV	– levofloxacin
AMK	– amikacin
CMP	– capreomycin
UPGMA	– unweighted pair group method with arithmetic average
HGDI	– Hunter-Gaston discriminatory index

Ethical statement

The study was approved by the Ethics Committee of the First Affiliated Hospital of Nanchang University (No. 2018015) and the Jiangxi Chest Hospital Institutional Review Board (No. 2018007). We confirmed that all informed consent was obtained from all participants, all information was anonymized, and no individual information could be identified.

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Authors' contributions

KC conceived and designed the experiments. DL, SY, JZ, QC and LY performed the experiments. QC did the data analysis. DL wrote the initial paper. All authors read and approved the final manuscript.

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Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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