Strategies to control drug-resistant tuberculosis transmission in China

A series of cross-sectional studies of patients diagnosed with drug-resistant TB was conducted over an 8-year period in rural areas of eastern China to understand the degree of recent TB transmission and to determine associated risk factors.

Key words
Beijing family, BCG vaccination, clustering, drug-resistant tuberculosis, eastern rural China, fluoroquinolones, isoniazid, *Mycobacterium tuberculosis*, resistance

Results
The proportion of tuberculosis (TB) cases due to recent transmission was estimated at 23.1% (32.1% W-Beijing genotype vs. 2.8% non-W-Beijing genotype). The relatively low clustering proportions highlight the role of endogenous reactivation of TB as a main concern in rural eastern China [1].

W-Beijing strains were associated with recent transmission in this population, where multidrug resistance and Bacille Calmette Guerin (BCG) vaccination may play an important role in TB transmission [1].

The relatively low level of clustering among fluoroquinolones (FQ)-resistant strains suggests that most of them are newly acquired, likely due to widespread FQ use [2].

These results highlighted that isoniazid-resistant *Mycobacterium tuberculosis* (Mtbc) (especially with a katG315Thr mutation) is likely to be clustered in a community, develop extra resistance to rifampicin and become multidrug-resistant TB (MDR-TB) in Chinese rural settings [3,4].

Policy considerations
- Complement Directly Observed Treatment, Short-course (DOTS) with additional strategies, e.g. case finding at the village level, treatment for patients with cavities and drug susceptibility testing for patients at increased risk for drug-resistance.
- Expand contact investigation of TB in rural China beyond household contact tracing, which may not be enough.
- Control the use of FQ and isoniazid (INH) to prevent the spread of extensively drug-resistant tuberculosis (XDR) in rural China.
- Invest in vaccination research aiming at the replacement of the BCG vaccination.

Key messages
- Transmission of drug-resistant tuberculosis in eastern rural China is characterized by small clusters and limited geographic spread.
- Bacille Calmette Guerin vaccination may favor the transmission of W-Beijing family strains.
- Extensive control of the use of fluoroquinolones and isoniazid is needed to prevent the spread of drug-resistant tuberculosis.

"Information about transmission patterns of drug-resistant tuberculosis could be important in decision-making for tuberculosis control."
Rationale of the study

The DOTS strategy has been implemented in China for 20 years, with 1.3 million infectious TB patients being provided with free anti-tuberculosis treatment in areas covered by DOTS. However, China still has the second highest TB burden in the world in terms of the number of cases.

Drug-resistance is associated with various factors, e.g. poor adherence to anti-TB treatment. MDR-TB comes about as a result of the stepwise accumulation of mutations in drug-resistance conferring genes. Recent studies have shown that drug-resistant TB is able to transmit and cause disease as often as drug-susceptible organisms. In addition to new acquisition, primary transmission of already resistant organisms may be fueling the ongoing MDR-TB epidemic.

Transmission patterns of drug-resistant Mtb may be influenced by differences in socio-demographics, local TB endemicity and efficaciousness of TB control programs. A better understanding of drug-resistant TB epidemiology is paramount to inform evidence-based control strategies for MDR-TB.

Methods

A series of cross-sectional studies of patients diagnosed with drug-resistant TB was conducted over an 8-year period in rural areas of eastern China with varying lengths of DOTS implementation. The demographic, clinical and epidemiologic information was combined with IS6110-based restricted fragment length polymorphism (RFLP) and Spoligotyping analysis of Mtb isolates. In addition, we conducted DNA sequencing of resistance determining regions to first-line anti-tuberculosis agents.

Inclusion criteria were active TB cases who were bacteriologically confirmed by sputum culture, and who consented to participate in the study. Extrapulmonary TB cases were excluded.

Patients were interviewed at the time of their TB diagnosis. The interview was conducted at the county TB dispensaries by physicians who had undergone a 2-day training course for the interview. A semi-structured questionnaire was developed that covered general demographic and socioeconomic characteristics, clinical symptoms and disease history at TB diagnosis. BCG vaccination was determined by self-report and confirmed by the presence of a scar at interview.

Selected literature


Correspondence

Weibing Wang, Associate Professor PhD
School of Public Health, Fudan University,
Shanghai, China

Biao Xu, Professor MD MPH PhD
School of Public Health, Fudan University
Shanghai, China

Research brief created by
Olivia Biermann, MSc
olivia.biermann@ki.se