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Intra-familial transmission of drug-resistant tuberculosis: A case series of sibling contacts

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Abstract
Background: Drug-resistant tuberculosis (DR-TB) is a growing concern globally, particularly in high-burden countries like India. Household contacts of DR-TB patients, especially children and adolescents, are at high risk of acquiring infection and progressing to active disease.
Objective: This case series aims to document intra-familial transmission of MDR-TB among siblings in a low-resource household, highlight diagnostic and therapeutic challenges, and discuss public health strategies to mitigate household transmission.
Methods: A retrospective clinical review was conducted on three siblings—index case (24-year-old male) diagnosed with MDR-TB, and his two younger siblings (17 and 15 years)—who developed MDR-TB within two months of exposure. Clinical presentation, diagnostics, treatment modifications, and outcomes were analyzed.
Results: All three patients were confirmed as MDR-TB by molecular diagnostics. One sibling developed peripheral neuropathy, necessitating a switch from Linezolid to Delamanid. With nutritional support and regular follow-up, both younger siblings showed weight gain and clinical improvement.
Conclusion: The case series underscores the critical importance of early contact screening, prompt diagnosis, and family-centered care in preventing morbidity from intra-familial DR-TB transmission. Strengthening national strategies like IPT and 3HP for household contacts remains essential.

Keywords: Drug-resistant tuberculosis, household contacts, mdr-tb, sibling transmission, preventive therapy, India, NTEP

Introduction
Drug-resistant tuberculosis (DR-TB) remains one of the most serious public health threats globally and particularly in high-burden countries like India. Despite significant advancements in diagnosis and treatment, the transmission of DR-TB within households continues to be a challenge due to delayed diagnosis, close proximity, and inadequate infection control. The risk of intra-familial transmission, especially among vulnerable populations such as children and adolescents, is heightened in overcrowded settings. This case series highlights a cluster of DR-TB among siblings, illustrating the clinical complexities, public health implications, and the importance of timely preventive interventions.

Overview
Household contact with a DR-TB case is a known high-risk factor for subsequent development of active TB, especially among children and immunocompromised individuals. In India, where DR-TB burden is rising, such cases represent sentinel events warranting immediate public health action. National and international strategies, including the WHO End TB Strategy and India's National Tuberculosis Elimination Program (NTEP), emphasize the importance of contact tracing, preventive therapy, and early treatment initiation to curb community spread. The emergence of DR-TB in adolescents in this series underscores a need for strengthened surveillance and community awareness.

Background
Household contacts of DR-TB cases are at significantly higher risk of latent TB infection (LTBI) and progression to active disease due to prolonged exposure. Studies from India have shown transmission rates ranging from 30–50% among close contacts, with higher rates in low-income settings where overcrowding, undernutrition, and delayed treatment contribute to transmission dynamics. The 2020 WHO Consolidated Guidelines on TB Preventive Treatment now recommend contact investigation and the use of newer preventive therapy regimens. The NTEP has introduced guidelines for contact screening and provision of Isoniazid Preventive Therapy (IPT) or newer options like 3HP (isoniazid + rifapentine) for eligible household contacts.
This case series describes three siblings in a low-resource household setting in Mumbai: the index case, a 24-year-old male diagnosed with MDR-TB; his younger sister (17 years) and brother (15 years) were diagnosed within months with the same strain, confirmed by molecular diagnostics. One sibling developed adverse drug reactions (peripheral neuropathy) requiring modification of the regimen. The clinical trajectory and successful management illustrate the importance of prompt diagnosis, flexible treatment regimens, and family-centered care.

Academic Discussion
Intra-household transmission of DR-TB reflects the failure of early identification and preventive strategies. Studies such as Shah *et al.* (2017, Clinical Infectious Diseases) [4]. and Atre *et al.* (2019, PLoS ONE) [3]. have documented clusters of DR-TB transmission in families and slum dwellings in India. Factors like poor ventilation, stigma delaying health-seeking behavior, and lack of awareness further compound the situation. Molecular epidemiology studies using genotyping and Whole Genome Sequencing

(WGS) have confirmed clonal transmission in multiple Indian clusters.

Globally, similar patterns have been reported in South Africa, Peru, and the Philippines. The WHO recommends contact investigation followed by tailored preventive therapy for those exposed to MDR-TB. However, limited rollout of such interventions, especially in resource-constrained countries, hampers progress.

The NTEP addresses household contacts as a key strategic pillar. Its recent initiatives include:

- Systematic screening of all household contacts of DR-TB patients
- Use of GeneXpert as the initial diagnostic tool
- Preventive therapy using INH or 3HP in eligible contacts (especially children <5 years and immunocompromised)
- Monthly follow-up for contacts for 6–24 months
- Nutritional and psychosocial support packages under Nikshay Poshan Yojana

In the presented case, timely diagnosis, switching of Linezolid to Delamanid after ADR, and comprehensive follow-up demonstrate the effectiveness of a patient- and family-centered approach in DR-TB control.

Methods

This case series involved a retrospective clinical review of three biologically related siblings residing in a single low-income household in Mumbai, India. The study aimed to analyze patterns of intra-familial transmission, clinical manifestations, treatment protocols, and outcomes of drug-resistant tuberculosis (DR-TB) in a real-world setting.

Study Population

The study focused on

- **Index case:** A 24-year-old male diagnosed with multidrug-resistant tuberculosis (MDR-TB).
- **Sibling 1:** A 17-year-old female who developed similar respiratory symptoms within two months of the index case's diagnosis.
- **Sibling 2:** A 15-year-old male who also developed respiratory symptoms in the same timeframe.

All three individuals shared the same one-room dwelling, had close physical contact, and reported no history of TB in the immediate months preceding the index case diagnosis.

Clinical Evaluation and Diagnosis

- Initial Symptomatology included persistent cough, weight loss, fever, and breathlessness in all three individuals.
- Sputum samples were collected for Acid-Fast Bacillus (AFB) smear microscopy, CBNAAT (GeneXpert MTB/RIF), and culture-based drug sensitivity testing.
- All three siblings tested positive for Mycobacterium tuberculosis, with rifampicin resistance confirmed by GeneXpert, indicating MDR-TB.
- Baseline blood investigations, chest X-rays, and liver and renal function tests were conducted.
- Electrodiagnostic screening was performed in Sibling 1 after reporting tingling and numbness in the lower limbs during the intensive phase of treatment.

Treatment Protocol

- All patients were initiated on the All-Oral Longer MDR-TB Regimen, as per the 2021 NTEP guidelines.
- The standard regimen included Bedaquiline, Levofloxacin, Linezolid, Clofazimine, and Cycloserine.
- After two months, Sibling 1 developed peripheral neuropathy likely due to Linezolid toxicity. Linezolid was promptly discontinued, and Delamanid was added as a substitute.
- Nutritional support was provided under the Nikshay Poshan Yojana, along with psychosocial counselling.

Follow-up and Outcome Monitoring

- Patients were monitored monthly for
- Weight gain, symptom regression, and treatment adherence.
- Laboratory monitoring for drug toxicity, especially hepatic and neurological side effects.
- Clinical well-being, especially in the adolescent patients.
- Treatment adherence was ensured through Directly Observed Therapy (DOT) and supported by family health workers.

Comparative Clinical Discussion

The three sibling cases underscore several critical aspects of drug-resistant tuberculosis management in household contacts:

1. **Vulnerability of Household Contacts:** Children and adolescents, due to their immature immune systems and prolonged exposure in congested households, are highly susceptible.

2. **Early Symptom Recognition and Diagnosis:** The timely diagnosis in the younger siblings within 2 months of the index case reflects effective household contact tracing.

3. **Treatment Adaptability and ADR Management:** The emergence of peripheral neuropathy due to Linezolid demonstrates the importance of vigilant ADR monitoring and timely regimen adjustment.

4. **Weight Gain as a Positive Prognostic Marker:** Improved appetite and clinical well-being during follow-up suggests effective treatment and good adherence.

5. **Psychosocial Support:** Nutritional and emotional support under Nikshay Poshan Yojana facilitated treatment success.

Implications for Public Health Practice

- Reinforce Contact Tracing and early molecular diagnostics.
- Strengthen Preventive Therapy Programs like IPT and 3HP.
- Promote Family-Centered Care and nutritional support.
- Enhance Surveillance using digital tools like Nikshay.

Take-Home Messages

Message for the Community

Protect Your Family—Act Early Against TB

If someone in your family has drug-resistant TB (DR-TB), it's essential to act fast. Children and teens in the same home are at high risk of getting infected. Don't ignore cough, weight loss, or fever—these may be early signs of

TB. Visit a TB center immediately for check-up and free treatment.

- **Get Tested:** All close family members should be screened for TB.
- **Protect Your Children:** Early preventive treatment can stop TB before it starts.
- **Follow Doctor's Advice:** Taking all medicines regularly cures TB—even drug-resistant TB.
- **Nutrition and Support Matter:** Good food and emotional support help healing.

Let's break the chain of TB—together as a family.

Message for Healthcare Workers

Household Contact Tracing is TB Prevention

This case series emphasizes the urgent need for systematic screening of all household contacts of DR-TB patients. Adolescents, especially siblings of index cases, are highly vulnerable and must not be overlooked.

- **Screen early and proactively:** Use CBNAAT as the frontline tool.
- **Initiate preventive therapy:** (IPT/3HP) for eligible contacts.
- Monitor closely for adverse drug reactions like Linezolid-induced neuropathy.
- Counsel the family and ensure DOTS adherence.

Every DR-TB contact diagnosed and managed early is a break in the transmission chain. You are key to ending TB.

Message for General Awareness

TB Spreads in Families—But So Does Protection

If one person in your home has TB, others may catch it too—especially drug-resistant TB. But TB is not a curse—it is treatable and preventable.

- **Know the early signs:** cough, weight loss, fever, weakness.
- **No delay in check-up:** Even healthy-looking children may have early TB.
- **Newer treatments work well:** Even drug-resistant TB can be cured.
- TB care is free under the Government's TB program.

Speak up, act early, and protect your family from TB.

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