

# Prevalence and Patterns of Drug-Resistant Tuberculosis in Patients Receiving Drug Sensitive Anti-Tubercular Medications within and Outside the DOTS at Nodal DRTB Center, SNMC, Agra

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**Abstract:** ***Introduction:** Drug-resistant tuberculosis is a major public health problem throughout world. India accounts for 27% of global TB burden. More than half of TB patients in India are cared for in private sector. Usage of inappropriate TB diagnostic, treatment practices and lack of adherence to ISTC continues to be documented among private practitioners, potentially contributing to delays in TB diagnosis, development of drug resistance, and ongoing TB transmission. **Objectives:** 1) To estimate Prevalence of Drug-Resistant Tuberculosis among those receiving DSTB regimen within and outside DOTS. 2) To study the Patterns of Drug-Resistant Tuberculosis among those receiving DSTB regimen within and outside DOTS. 3) To compare Prevalence and Patterns of Drug-Resistant Tuberculosis among those receiving DSTB regimen within and outside DOTS. **Materials and Methods:** Hospital-based, prospective observational study, performed at tertiary care center, Agra on patients receiving DSTB medications in both within and outside DOTS category. Sputum specimens collected, Rapid molecular drug-resistance testing and growth-based drug-susceptibility testing (DST) were performed. **Results:** Prevalence of DRTB within the DOTS category 8.16% and outside the DOTS category 10.88% obtained. RR, MDR, PRE XDR and XDR rates are higher in the category of Outside DOTS and the H mono/poly resistance pattern is higher among the Within the DOTS category. **Conclusions:** Prevalence rates of DRTB are more in outside the DOTS category with high statistical significance and Pre-XDR and XDR forms of DRTB is more in the category of outside DOTS than within DOTS and need further studies to properly explore data and suggest better policies in public private partnership to achieve the ambitious goal of Tuberculosis elimination.*

**Keywords:** Drug-resistant tuberculosis; Extensively drug-resistant tuberculosis, National tuberculosis elimination program; Within DOTS, Outside DOTS

## 1. Introduction

Drug-resistant TB (DR-TB) continues to be a public health threat. Resistance to Rifampicin, the most effective first-line drug – is of greatest concern. In 2021, the estimated proportion of people with TB who had MDR/RR-TB was 3.6% among new cases and 18% among those previously treated. (1) Private practitioners are frequently the first point of healthcare contact for patients with tuberculosis (TB) in India. Inappropriate TB management practices among them may contribute to delayed TB diagnosis and generate drug resistance (3,4).

Although the Government of India's National TB Elimination Program (NTEP) provides free TB healthcare services, TB-related symptoms in urban Indian settings first seek healthcare from private practitioners and about 50% ultimately get TB treatment outside the NTEP (2).

However, usage of inappropriate TB diagnostic and treatment practices and lack of adherence to ISTC continues

to be documented among private practitioners, potentially contributing to delays in TB diagnosis, development of drug resistance, and ongoing TB transmission.

In order to achieve the targeted goal of TB elimination from India by 2025, 5 years ahead of global elimination plan further research, as well as an up-to-date assessment of the TB epidemic at all the levels required (5).

Our study with the objectives to determine the prevalence and patterns of Drug Resistant Tuberculosis (DRTB) among those receiving DSTB regimen within and outside DOTS and Compare the prevalence and patterns of drug resistance in both populations, was an attempt to suggest the betterment of existing elimination strategies.

## 2. Material and Methods

A hospital-based, observational prospective study, conducted from January 2021 to June 2022 at nodal DRTB center, department of TB & Respiratory Diseases S. N.

Medical College Agra with below-mentioned criteria.

#### Inclusion criteria

- Persons with informed consent.
- Newly diagnosed smear-positive pulmonary Tuberculosis patients on DSTB regimen
- Sputum smears positive Patients on outside DOTS treatment.

#### Exclusion criteria

- Pulmonary TB patients who are registered under DOTS outside period of study.
- Extrapulmonary Tuberculosis.
- Previous treatment of MDR or XDR. Participants have been subjected to clinical history, examination and information obtained about demographic features and Previous history of TB or anti-TB Drug intake, or any preventive therapy and if present the drugs used, etc., and subjected to investigations like CBNAAT, Line Probe Assay. Drug Susceptibility Testing (DST), Chest X-ray, etc.

The STTDC, Agra, is a Central TB division-certified Culture and drug-susceptibility test IRL laboratory and is well-equipped with molecular diagnostics like CBNAAT and LPA.

Result of the CBNAAT was available as (I) MTB—detected/not detected and (II) rifampicin resistance—detected/not detected/ indeterminate. Rifampicin resistance detected (by CBNAAT) sputum specimens were subjected to a first line-line and second line-line probe assay, and liquid culture-drug susceptibility testing (LC-DST).

R-R not detected by CBNAAT subjected to FL-LPA, and if H (isoniazid) resistance was detected by FL-LPA, then subjected to SL-LPA LC-DST.

**Statistical analysis of data:** Statistical analysis was conducted with SPSS 20 software. P value <0.05 was considered statistically significant for the tests applied like chi square, Fisher exact and regression models.

### 3. Results

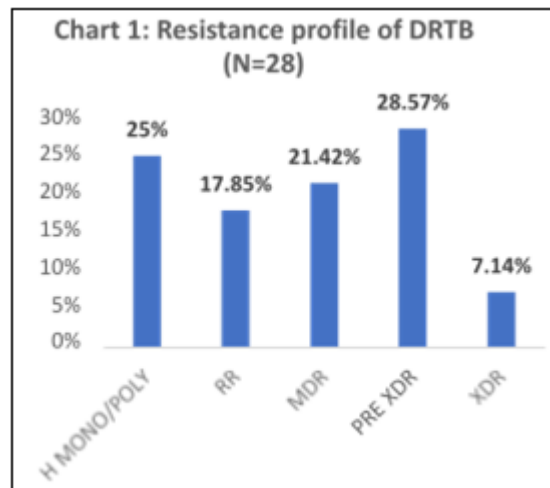
Study was done on cohort of 147 patients and approximately half were males and half females, with mean age of 31.6 years with majority of patients being in younger age group. 32.65% were severely undernourished with the body mass index below 16.68.69% study population had personal habits such as tobacco and alcohol consumption. 42.85% were categorized in class IV (Upper lower) of kuppuswamy scale. 33.33% originated from the private and 66.66% belong to the Government sector.

#### Patterns of Drug Resistance:

Among 147 smear-positive pulmonary tuberculosis on DSTB regimen subjected to CBNAAT, 21 (14.28%) were diagnosed as rifampicin-resistant (RR), whereas 126 (85.71%) were rifampicin-sensitive (RS).

All 21 rifampicin-resistant tuberculosis patients subjected to

FL-LPA, SL-LPA, and LC-DST. MDR/RR-TB was detected in 19 patients and XDR-TB was detected in 2 patients. Among the MDR/RR patients, 11 had no additional resistance to the fluoroquinolone (FQ) or second-line injectable-drug (SLID); while 10 patients had additional resistance to the FQ/SLID (8 MDR/RR-TB had additional resistance to the FQ and 2 MDR/RR-TB with additional resistance to the SLID).

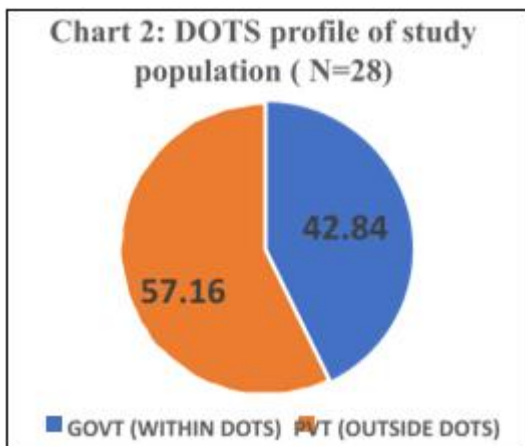


126 rifampicin-sensitive patients subjected to first line-line probe assay.<sup>7</sup> in whom H-mono/poly-drug-resistance detected were subjected to a second line-line probe assay and liquid culture—drug susceptibility testing, out of these, 5 patients had no additional resistance to the fluoroquinolone (FQ) or second-line injectable-drug (SLID) class, while 2 had additional resistance to the fluoroquinolone (FQ).

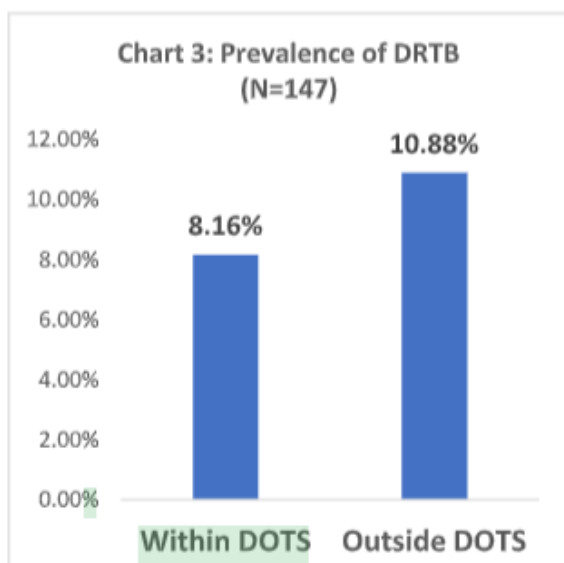
### 4. Discussion

In our study 53.57% of the patients were in the age group of 18-25 years. Mean age was 30.6 years; similar to studies conducted in public sector (6, 7, 8). High prevalence of DR-TB in young population is alarming as this would result in considerable health and financial burden. (9)

Among study population, 49 (33.33%) were from private (Outside DOTS) and 98 (66.77%) public sector (Within DOTS). As per the reports of DST and LPA total of 28 (19.04%) patients were found to have DRTB. Among these 12 (42.84%) were within the DOTS and 16 (57.16%) outside DOTS.



Prevalence of DRTB within DOTS category 8.16% and outside DOTS is 10.88%.



Overall prevalence of 19.04% obtained and 8.16% within DOTS and 10.88% outside the DOTS category and results of the study match with study conducted by Dawit Asmamaw et al in Addis Ababa, Ethiopia obtaining the prevalence of 10.4% for newly diagnosed DRTB in smear-positive patients in the public sector (10) and that of the study conducted by Jain A et al at Lucknow Uttar Pradesh India obtaining Overall Prevalence of MDR 19.8 percent (11).

We have not come across any specific study of estimation of prevalence and patterns in the private sector in country or abroad and our finding that patients outside DOTS have more prevalence is supported by various studies carried out in the private sector with respect to prescription practices and some of the documents of National importance in the field of Tuberculosis (12). The data outside DOTS from the private sector is higher than that of the public sector 10.88% may be due to delayed diagnosis, suboptimal quality of care, incorrect diagnostic & treatment protocols, lack of systems for treatment adherence and a high drop-out rate due to illiteracy, ignorance, and financial constraints, raising risk of drug resistance to first-line or second-line drugs (13).

Inappropriate prescribing patterns related to active TB disease in the private health sector and easy/over-the –

counter access to fluoroquinolones both contribute to the pool of DRTB patients. Findings are same in a study conducted by Alpa Dalal et al in Mumbai (6) Among 28 patients 12 (42.84%) were within DOTS and 16 (57.16%) were outside DOTS. Among them the drug resistant profiles are as follows H MONO/POLY 7 (25%), RR 5 (17.85%), MDR 6 (21.42%), PRE XDR 8 (28.57%), and XDR 2 (7.14%). Results are in concordance with study conducted by Vishal Prakash Giri et al in eastern parts of India. (5) and Yuanping Pan et al in Dalian, China (13).

The monoresistance to rifampicin was detected in 7.14%. This is higher than the Studies conducted in Ethiopia quoting the ranges from 0% to 1.9% and other parts of India (1.1%)

Myanmar (2%) and Cameroon (2.1%).

HIV seropositivity, Diabetes and Low BMI also acts as risk factors for rapid progression from DSTB to DRTB as reflected by various other studies (11, 12, 13).

## 5. Limitations

An extensive search online and manually at various standard academic institutions we could not get a study where specific estimation of prevalence and patterns in private sector and that limit us to compare and obtain inference with respect to the category of outside DOTS population. In order to infer and draw conclusions we relayed mainly on global, national, and regional reports.

## 6. Conclusions

Prevalence of DRTB more in private sector (outside the DOTS), need further studies in the field to properly explore data to suggest better policies for health in the field of public-private partnership to achieve the ambitious goal of TB elimination.

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