

Status of Universal Drug Susceptibility Testing in Pulmonary Tuberculosis Patients Initiated on Treatment in an Urban Setting, South India

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Abstract

Introduction: Early initiation of drug susceptibility testing (DST) guided anti-tuberculosis treatment benefits the patient in terms of better treatment outcomes and possibly reduces the transmission of tuberculosis (TB) disease in the community. To determine the status of universal DST (UDST) coverage in smear-positive pulmonary TB patients (PTB) initiated on treatment under the TB program in Greater Chennai Corporation. In addition, the barriers and facilitators for UDST were explored. **Material and Methods:** The data of PTB patients who were initiated on anti-TB treatment from July to December 2019 was abstracted from the NI-KSHAY database of TB Program. The barriers and facilitators for UDST were explored in 5 focus group discussions (FGDs) among the TB program healthcare workers (HCW). UDST coverage was based on the availability of Cartridge-based Nucleic Acid Amplification test (CBNAAT) results in the NI-KSHAY database. **Results:** The CBNAAT result was available for 1628 (82.6%) of the 1970 smear-positive PTB patients. Non-availability of CBNAAT results was significantly higher among the older age group (>50 years), in female PTB patients, and the Private Sector. Issues with sputum collection, transport of specimens, and receipt of results were highlighted by the HCWs for the non-availability of UDST results. **Conclusion:** Universal DST coverage in smear-positive PTB patients initiated on treatment in 2019 in Chennai was optimal as per National Strategic Plan for TB elimination UDST target of 80% for the year 2020 but with scope for improvement. The low UDST coverage in the private sector, among female patients and older age groups, needs to be addressed.

Keywords: Chennai, CBNAAT, private sector, pulmonary TB, UDST

INTRODUCTION

Universal drug susceptibility testing (UDST) is an important component of the Integrated patient-centered care and tuberculosis (TB) prevention pillar of the end TB strategy.^[1] Worldwide, 71% of people diagnosed with bacteriologically confirmed pulmonary TB were tested for rifampicin resistance in 2020, which was an increase from 61% in 2019.^[2] In India, the UDST coverage increased from 58% in 2019 to 67% in 2020.^[3] The integrated drug-resistant TB (DR-TB) algorithm of the National TB Elimination Programme (NTEP) is a strategy to ensure that DST is offered to TB patients early in the diagnostic process for initiation of appropriate anti-TB treatment.^[4] As per NTEP, the cartridge-based nucleic acid amplification test (CBNAAT) is offered to all diagnosed

smear-positive PTB patients. Those with Rifampicin resistance not detected in CBNAAT will have to undergo a line probe assay (LPA) test for first-line drugs namely Isoniazid (INH) and or Rifampicin (RIF) primarily to rule out INH resistance. Patients with RIF resistance detected in CBNAAT and those with INH and/or RIF resistance detected in first-line LPA will

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have to undergo second-line LPA testing and culture drug susceptibility testing for further drug resistance.^[4]

Early initiation of DST-guided anti-TB treatment benefits the patient in terms of better treatment outcomes and possibly reduces the transmission of TB disease in the community. The objective of the study was to determine the status of universal drug susceptibility testing in smear-positive pulmonary TB patients initiated on treatment under NTEP. In addition, the barriers and facilitators for drug susceptibility testing were explored.

METHODS

The study was done during the period from April 2019 to September 2021. Greater Chennai Corporation, an urban setting with a population of 11.2 million is in the State of Tamil Nadu. The division of Chennai Corporation for NTEP management includes 5 districts – North, South, East, West, and Central Chennai. The study population for UDST coverage included smear-positive pulmonary TB patients initiated on anti-TB treatment from July to December 2019. Focus group discussion (FGD) was conducted among the NTEP Health Care Workers involved in sputum collection, examination, and reporting procedures. The data on smear-positive pulmonary TB patients were abstracted from NI-KSHAY which is the TB Surveillance database of NTEP. Information on age, gender, type of sector (Public/Private), type of TB case [pulmonary TB (PTB)/Extra-pulmonary TB (EPTB)], CBNAAT, LPA tests, and results were abstracted. A total of 5 face-to-face FGDs (one per division of Chennai) each with 8 senior treatment laboratory supervisors (STLSs) and laboratory technicians (LTs) selected based on convenience was conducted. Written informed consent was obtained before FGD. The FGDs which lasted for approximately 45–60 min were facilitated in the local language by a certified and trained social worker and public health researcher. Participants were asked to discuss their experiences in UDST, perceived difficulties, and barriers in implementation with a specific focus on sputum collection, transportation of sputum specimens, reporting, and receipt of results. Probes were first pilot tested with a small number of participants and were refined in terms of phrasing and sequencing. The audio recording was done and notes were taken separately by a note taker. Trained staff visited the Designated Microscopy Centre (DMC), treatment center, and CBNAAT centers with a semi-structured facility survey form. Details on outpatient services, chest x-ray and staff availability, laboratory services, electrical power back-up, access to the internet, and modality of transport of sputum specimens were collected. Universal DST coverage was based on the availability of CBNAAT results in the NI-KSHAY database. Data were analyzed using STATA Version 15.1. Proportions were computed for quantitative variables. Statistical difference in distributions of proportions between those with and without CBNAAT results was determined using the Chi-square test. Statistical significance was determined at 5%. Notes from FGD were transcribed from the local language and translated into

English ensuring linguistic nuances and quality. The analysis was conducted manually, using a pre-determined set of codes. A deductive approach was used to arrive at preliminary themes and broad themes. The consensus was arrived at wherever there was disagreement on themes. The study was approved by the National Institute for research in Tuberculosis Institutional Ethics Committee.

RESULTS

Availability of facilities at the DMC, treatment, and CBNAAT centers

There were a total 156 DMCs with 99 functioning as treatment centre, 17 with CBNAAT centre and one LPA testing facility that provided TB services to the population of Chennai District in 2019. During the period of the study, over 90% of the centers offered out-patient services and sputum microscopy testing with the availability of doctors and lab technicians [Table 1]. The availability of chest x-ray facilities within the premises of the centers ranged from 10% to 35%. The labelling of sputum specimens was appropriate in all centres while the mechanism of transport of sputum specimens in 3-layer packaging material was followed in 52% to 76%. There were over 90% of the centers with access to the internet while power backup for electricity was available in 20% to 76% of the centers.

Status of drug susceptibility testing for smear-positive PTB patients

There were 8417 TB patients initiated on anti-TB treatment as per the NI-KSHAY database from July to December 2019 of which pulmonary TB (PTB) constituted 5842 (69.4%). Sputum smear result was available for 2640 PTB patients of which 1970 (74.6%) were sputum smear positive.

The CBNAAT result was available for 1628 (82.6%) of the 1970 smear-positive PTB patients [Figure 1]. Of 1474 who were eligible for First line LPA, the results were available for 549 (37.2%) patients. There were 95 patients eligible for second-line LPA testing of which the results were available for 34 (38.9%).

Drug susceptibility testing based on age, gender, and sector (public/private)

A comparison of age, gender, type of sector, and division of Chennai in PTB patients based on CBNAAT data availability is shown in Table 2. Among those with non-availability of data for CBNAAT, a significantly higher proportion was aged beyond 50 years (44.8%) [$p < 0.001$], female patients (29.5%) [$p = 0.002$], and private sector PTB patients (58.8%) [$p < 0.001$]. PTB patients from Central, East, and West Chennai divisions had higher CBNAAT data non-availability ($p < 0.001$).

Excerpts from focus group discussion among the healthcare workers

There were 34 LTs, 8 STLS, and one technical officer who participated in FGD. Their mean years of service was 7.4 years (range 6 months to 20 years).

Table 1: Facilities available at the Designated Microscopy Centre (DMC), treatment centers, and CBNAAT centers in Chennai

	DMC n=40		DMC + Treatment center n=99		DMC + Treatment + CBNAAT center n=17	
	n	%	n	%	n	%
Out-patient services offered	40	100	97	98	16	94
Chest X-ray facility available	4	10	21	21	6	35
Sputum microscopy testing services offered	38	95	95	96	16	94
Treatment for TB provided	6	15	96	97	17	100
Availability of access to internet	38	95	93	94	16	94
Availability of electricity power back-up	8	20	46	46	13	76
Doctor visits the clinic regularly	40	100	97	98	17	100
Lab technician available	39	97	95	96	16	94
Sputum specimen labeled appropriately	40	100	97	98	17	100
3-layer packaging material used for sputum specimen transport	21	52	70	71	13	76

CBNAAT - Cartridge-based Nucleic Acid Amplification test

Overall experience with implementation of DST

The HCW felt that implementation of DST identified drug resistance early for appropriate treatment; however, there are challenges in its implementation

‘We can find the drug-resistant cases early and thus can start the right treatment immediately. Earlier we had to wait long to know whether the drug is resistant or not’

‘After implementing the DST method, we are facing lots of issues related to work such as collecting the extra samples, documenting, and transporting the samples’

Challenges in the implementation of DST

Sputum collection

The difficulty in collecting additional sputum specimens for DST was highlighted by the HCW.

‘Patients are having difficulties or not willing to give three samples because most of the patients complained of not being able to produce sputum and that it is impossible for them to give three samples’

‘Sometimes we have difficulties in collecting sputum from the patients who have been referred from private hospitals. They say that they don’t want extra tests and they are not allowing us to collect the sputum at home also. Even if we give counseling also they are not accepting to do the test and sometimes private hospital doctors also explain the patients to do the sputum test. Even then also they won’t accept to do the test’

Sputum transportation

Transportation of sputum specimens to the CBNAAT/LPA laboratory is challenging for the HCWs in terms of supplies, workforce, workload.

‘We don’t have many CBNAAT/LPA centers, so we must transport samples’

‘We store 4 to 5 samples in one zip lock cover to transport the samples and sometimes we use normal plastic covers. We don’t have a person to transport the sample and because of this, we are finding it difficult to transport the samples especially

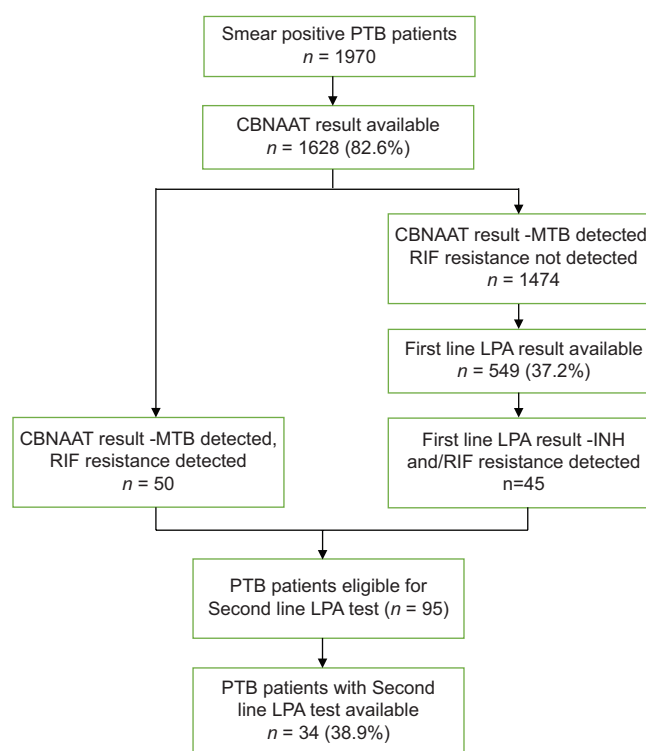


Figure 1: Status of drug susceptibility testing for smear-positive pulmonary tuberculosis (PTB) patients initiated on treatment from July to December 2019 in Chennai. CBNAAT – Cartridge-based Nucleic Acid Amplification test; LPA – Line Probe Assay; INH – Isoniazid; RIF - Rifampicin

sometimes when the samples get damaged and when we need to collect samples again’

‘They think that just for one sputum sample why they have to go, so they wait for three or four sputum and then they take it to the centre, so the sputum results are getting delayed’

Receipt of DST results

The delay in receipt of results for LPA was mentioned by the HCWs.

‘We don’t have any problem with getting results from CBNAAT center’

Table 2: Comparison of smear-positive pulmonary tuberculosis (PTB) patients based on data availability for CBNAAT

Characteristics	CBNAAT data				P*
	Available n=1628		Not available n=342		
	n	%	n	%	
Age in years					
0-17	38	2.3	12	3.5	<0.001
18-30	242	14.9	62	18.1	
31-40	321	19.7	56	16.4	
41-50	445	27.3	59	17.3	
51-60	368	22.6	85	24.9	
>60	214	13.1	68	19.9	
Gender					
Female	341	20.9	101	29.5	0.002
Male	1284	78.9	241	70.5	
Transgender	3	0.2	0	0	
Type of Sector					
Private	34	2.1	201	58.8	<0.001
Public	1594	97.9	141	41.2	
Division of Chennai					
Central	630	38.7	145	42.4	<0.001
East	370	22.7	94	27.5	
North	334	20.5	26	7.6	
South	155	9.5	19	5.6	
West	139	8.5	58	17	

*Chi-square test. CBNAAT - Cartridge-based Nucleic Acid Amplification test

'We are not receiving the results properly for LPA and sometimes it takes 2 to 3 months. After one month we receive complaints stating that the samples are damaged. So, we are finding it difficult to obtain results'

'We are getting the LPA results together (Overall Chennai, Tiruvallur, and Kanchipuram districts) so we have difficulties searching and finding our patients' results'

Communication of results to patients/providers

The modality of communication of DST results includes mobile communication and email.

'We inform the results to the HV who calls up the patients/providers and informs them about the results. If the patient's phone number is not available, the HV does a home visit and discloses the results to the patient. For providers, we are using official mail IDs, in which we share the results'

Recommendations to improve implementation of DST

The need for manpower, coordination among staff, adequate specimen transport supplies, a user-friendly format of receipt of results, and additional CBNAAT, and LPA centers were suggested by the HCWs.

'We need the LPA results zone wise so that it will be easy to find. Also, arrangements for some manpower for transporting sputum samples will be helpful'

'Need proper materials and supplies for sputum transportation'

'Proper communication between LTs, HVs, and coordinators'

'Need for more CBNAAT/LPA centres'

DISCUSSION

The coverage for UDST based on the availability of CBNAAT results in the NIKSHAY database was 82.6% for smear-positive PTB patients in Chennai. The UDST coverage in 2019 was 68% in Tamil Nadu which increased to 82% in the year 2020.^[3] As per the National Strategic Plan for TB elimination in India, the target for the proportion of notified TB patients to be offered DST is 80%, 98%, and 100% for the years 2020, 2023, and 2025 respectively.^[5] Our findings suggest that the UDST coverage for PTB patients initiated on treatment during 2019 is optimal in Chennai. However, the coverage for LPA testing was about one-third which requires improvement. Studies have documented that rapid molecular diagnostic tests reduce the delay in treatment initiation in drug-resistant TB resulting in better treatment outcomes.^[6,7]

The UDST coverage in the private sector was low (14%) compared to the public sector (92%). The UDST coverage in the private sector in 2019 was 28% in India and Tamil Nadu.^[3] This is a matter of concern since about 50% of TB patients seek care in the Private sector.^[8] The difficulty in collecting sputum for UDST from patients referred from the private sector was highlighted by the HCWs during the FGDs. These findings underscore the importance of engagement with the private sector to ensure optimal UDST coverage. The higher non-availability of CBNAAT data for female PTB patients compared to males requires further exploration since gender differences in health-seeking behavior have been reported among TB patients.^[9] Likewise, the low availability of CBNAAT data in the older age group (>50 years) needs further evaluation.

The challenges in sputum collection and transport were highlighted by the HCWs. The few CBNAAT (n = 17) and LPA (n = 1) laboratories catering to the Chennai population pose operational challenges as sputum specimens have to be transported to these labs from the DMCs. Lack of materials for sputum transport, manpower issues, and delay in the receipt of LPA results need to be addressed to ensure optimal DST coverage. These challenges suggest the importance of DST availability at the point of care for the benefit of both patients and HCWs. The new diagnostic test Truenat MTB and MTB plus which has been endorsed by the World Health Organization (WHO) offers scope for DST at the DMCs.^[10]

The chest x-ray is a sensitive screening tool in the diagnosis of TB. It is important in the diagnosis of pediatric TB and TB among PLHIV. The chest x-ray is an early triage test in the diagnostic algorithm for the diagnosis of TB in India.^[11] The non-availability of chest x-ray in health facilities ranged from 90% to 65%. This implies that the presumptive TB patient has to travel to an alternate facility for an x-ray. This could

potentially delay the diagnosis of TB and cause financial burdens to the patient.

The study has some limitations as it was from the data entered in NI-KSHAY database and was not cross-verified for completeness with laboratory results. The turnaround time for the tests, delay in treatment initiation, details of treatment provided based on DST, and culture DST could not be analyzed due to the non-availability of appropriate data. The study did not capture patients' perspectives on undergoing DST.

CONCLUSION

We observed that the UDST coverage based on CBNAAT data availability in smear-positive PTB patients initiated on treatment in 2019 in Chennai was optimal as per National Strategic Plan for TB elimination UDST target of 80% for the year 2020. However, there is scope for improvement. The low UDST coverage in the private sector, among female patients and older age groups, needs to be addressed. Challenges in implementing UDST have to be identified and addressed for optimal use of molecular tests in TB to potentiate its intended benefits.

DECLARATION OF HEALTH CARE WORKER CONSENT

The authors certify that they have obtained appropriate consent forms from Health Care Workers (HCW). In the form, HCW has given his/her consent for his/her views to be reported in the journal. The HCWs understand that their names and initials will not be published and due efforts will be made to conceal their identity.

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Conflicts of interest

There are no conflicts of interest.

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