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Original Research Article.

Epidemiology of Drug Resistant Mycobacterium Tuberculosis in Bengaluru City, Karnataka: A Cross Sectional Study

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ABSTRACT

Background: As estimated by WHO, India is having 27% of the world's drug resistant TB cases. To achieve the goals of End-TB Strategy, adequate information on the epidemiology of DR TB is required routinely to ascertain its burden, area of aggregation, trends and future prediction modelling for implementation of early diagnosis and effective treatment management practices. The current study was aimed to determine the epidemiology of *Mycobacterium tuberculosis* in Bengaluru city, Karnataka, India.

Methods: This was a descriptive cross-sectional study using programmatic data among the notified TB cases during the year 2017-2020 under NTEP of Bengaluru city. Socio-demographic data, clinical characteristics and diagnostic data were studied. Data analysis was conducted in Python (version 3.9.4) and ArcMap (version 10.8) was used to undertake the spatiotemporal analysis.

Results and Conclusions: A total of 37,984 TB cases were notified from 2017 to 2020. Among the total TB cases, 24,343 (64.1%) cases were microbiologically confirmed and remaining 13,641 (35.9%) were clinically diagnosed. Of the microbiologically confirmed TB cases overall 23,654 (97.2%) were drug sensitive TB cases and 689 (2.8%) were diagnosed as DR TB cases having resistance to any first line anti TB drug. The mean age of the DR TB patients was observed as 36.7 years (95% CI: 22.3-51.1). The burden of DR TB was highest in the key population groups. Out of the total DR TB cases, 412 (59.8%) cases were MDR RIF resistant, 268 (38.9%) were INH resistant, 66 (9.6%) were MDR and 8 (1.2%) were of XDR. The overall prevalence of DR TB during the study years was estimated at 6.5% (95% CI: 6.0 - 7.0). The study finding highlights the increasing trends of DR TB in Bengaluru city from 4.4% to 8.8% (p <0.001) out of the microbiologically confirmed TB patients diagnosed during 2017 to 2020. The study determine the DR TB hotspots identified by the geospatial analysis in the Bengaluru city further warranting the need of intensified Active Case Finding in the identified clusters. Thus, multipronged approach aiming on End TB strategy by improving diagnostic capacity, guaranteeing high-quality treatment and preventing transmission will be essential to restrict the challenge of DR-TB in India.

Keywords: Tuberculosis, DR TB, MDR RR TB, UDST, PMDT, NTEP, Epidemiology, Spatiotemporal Distribution, Bengaluru.

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INTRODUCTION

India is the second populous country in the world with one fourth of the global tuberculosis (TB) burden.[1] India rated at number one among the eight countries accounted for 66% of new TB cases in the year 2019.[2] About 40% of the Indian population is infected with TB bacillus.[3] In 2020, Incidence of TB in India was estimated at 25, 90,000 with 4,93,000 TB attributed deaths.[4] India bears second highest number of estimated HIV associated TB in the world. An estimated 53,000 HIV associated TB occurred in 2020 and 11,000 estimated number of patients died among them.[4]

As estimated by World Health Organisation (WHO), India is having 27% of the world's drug resistant (DR) TB cases in-spite of the availability of free of cost high quality diagnostic & treatment facilities under the Programmatic Management of Drug-resistant Tuberculosis (PMDT) services of National Tuberculosis Elimination Programme (NTEP). About 2.8% (2.3-3.5) of new TB cases and 14% (14-14) of previously treated TB cases are of Multi Drug Resistant (MDR)/Rifampicin Resistant (RR) TB.[2] In the year 2019, WHO estimated annual incidence of 1,24,000 (73,000-1,89,000) MDR/RR TB in India. Out of the estimated incidence, about 66,255 (53%) were laboratory confirmed and 56,569 (46%) were put on treatment under the PMDT.[2] This leaves 47% of estimated cases of the MDR/RR TB undiagnosed and 56% of estimated cases untreated. One of the barriers to access to treatment of DR TB is that management of TB is centralized and

over-reliant on hospitals thus stimulates towards wider decentralization of services and expansion of ambulatory models of care to increase the current MDR TB treatment success rate of 48% against 56% of global rate.[5]

India is a signatory of World Health Assembly (WHA) that endorsed Sustainable Development Goals (SDGs) and Global 'End TB Strategy' for a world free of tuberculosis with measurable aims of 50% & 75% reduction in incidence & TB deaths, respectively, by the year 2025, and corresponding reduction of 90% & 95% by the year 2035 as well as zero catastrophic expenditures due to TB.[6] To achieve this desired outcome, NTEP has developed an ambitious National Strategic Plan (2017-2025) in line with the National Health Policy, 2017.[7] Even though TB being a curable disease, besides the availability of newer diagnostics tools and standardized treatment regimens, the increasing resistance to anti-TB drugs in the form of drug resistant tuberculosis (DR-TB) is an evolving public health concern across the globe. In India, services under the PMDT were introduced in the year 2007 and nation-wide coverage was accomplished by the year 2013.[8]

In India, 21% of all TB notified cases are contributed by the private healthcare providers.[9] Most of the missing cases are assumed to be the patients treated by private healthcare providers and eventually never reported/notified under the NTEP. In addition, there is no concrete information on the use of Universal Drug Sensitivity Testing (UDST) among the privately notified cases. The gross implication is that the DR TB cases are remain missing, undiagnosed and untreated in the community. Eventually, many of these cases will die or continue to be sick and transmit the disease or, if treated with inadequate drugs, contribute to the increasing threat of drug resistance. Missing TB cases and DR TB together pose the foremost threats to NTEP.[10]

The treatment approach for patients with DR TB focuses under one roof sharing treatment care services along with drug sensitive patients during the initiation of treatment as well as during the complications management in our country. Several contributing factors such as previously treated/failure/relapse, TB-HIV co-infection, diabetes mellitus, socioeconomic status, drug/substance abuse, immunocompromised states *etc.* have been identified in the causation of DR TB.[11]

However, adequate information on the epidemiology of DR TB is required routinely to ascertain its burden, area of aggregation, trends and future prediction modelling for implementation of early diagnosis and effective treatment management practices. NIKSHAY (a web based case based monitoring system under NTEP) is in place to ensure effective monitoring of TB patients in India. The routine surveillance of programme through the programmatic data will highlight both its success and failure to find the weak areas that need additional interventions for better programmatic outcomes.[12]

There is a paucity of data on epidemiology of DR TB from Bengaluru as well as in the state of Karnataka, India. Bengaluru is administratively bifurcated into three districts *i.e.* Bengaluru urban, Bengaluru rural & Bengaluru city. Therefore, this study was conducted to determine the epidemiology of *Mycobacterium tuberculosis* in Bengaluru city, Karnataka. Bengaluru city covers maximum population of 8,749,944 under NTEP accounting for the highest numbers of all forms of TB cases than other districts in the state of Karnataka.[13]

OBJECTIVES

1. To find out the prevalence of drug resistant TB in Bengaluru city, Karnataka.
2. To identify the major factors associated with emergence of DR TB in Bengaluru city, Karnataka.
3. To observe the trends of drug resistant TB in Bengaluru city, Karnataka.
4. To undertake the spatiotemporal analysis of DR TB patients in the Bengaluru city, Karnataka.

MATERIALS AND METHODS

General Setting

Bengaluru city is the state capital of the Karnataka State. Bengaluru city jurisdiction covers all the geographical areas under Bruhat Bengaluru Mahanagara Palike (BBMP) that covers an area is 709 square kilometre. The population of Bengaluru city is 8.7 million with a sex ratio of 923 females to 1000 males with an estimated annual TB notification rate of 124per lakh population.[1,13]

Diagnosis of DR-TB

The guidelines under PMDT was followed for the diagnosis and treatment of DR-TB in the study area. During the year 2017, the criteria-C (Patients with presumptive MDR-TB included all 'previously treated' patients, any patient who was follow-up smear positive (FUS+), new patients with pulmonary TB who were contacts of known MDR-TB and all HIV-TB co-infected cases at diagnosis) was used for identifying presumptive MDR-TB patients.[14]

All the identified presumptive MDR-TB were offered both phenotypic (culture and drug sensitivity) and molecular (Xpert MTB/RIF assay) Drug Susceptibility Testing (DST) to detect resistance to the first line anti-TB drugs. From January 2018, Universal Drug Susceptibility Testing (UDST) was implemented in the study settings.[15] As per UDST guidelines, all the patients diagnosed for TB were to be offered upfront DST using Xpert MTB/RIF assay.[16]

DR-TB Treatment Initiation, Follow-Up and Treatment Outcomes

All the diagnosed DR-TB patients from the Bengaluru city included in the study were referred by the diagnostic sites to the DR-TB Centre, SDS - TRC & RGICD Campus, Bengaluru for pre-treatment evaluation and treatment initiation. The patients at the DR-TB centre were registered for treatment care with a distinctive DR-TB registration number. The socio-demographic and clinical profile, along with the address and contact numbers of the patient, were documented in PMDT card.

Subsequently, at the DR-TB centre, all the patients were evaluated and initiated on treatment. Patients were put on treatment with prescribed drugs ensuring the PMDT guidelines. After treatment initiation, patients were monitored at the DR-TB Centre, SDS - TRC & RGICD Campus, Bengaluru for 1 to 2 weeks. Once a patient is steady and able to endure the second-line drugs, then he/she was referred to the peripheral healthcare institution (PHI) nearest to the patient's residence locality for further care and periodical follow-ups at the PHI. All the records of the treatment course in the DR-TB centre including the referral details were updated in the DR-TB treatment card, DR-TB register and NIKSHAY portal. The PHI staff play an important role with regards to treatment care services and routine monitoring the patients throughout the treatment duration.

Diagnosis of DR-TB and Treatment by Private Providers

The DR-TB patients diagnosed by the private healthcare providers were notified to the NTEP as per the programmatic guidelines. Since, the treatment of DR-TB is complex, majority of the patients were initiated on treatment at the DR-TB centre and subsequently, refereed to PHIs in proximity of patient's residence for further treatment continuation. It is also assumed considering the out of pocket expenditures towards purchase of second-line anti TB drug's costs and availability, very few patients prefer to get the treatment from the private healthcare providers and majority of these patients seek treatment care services at public health care facilities.

Study Design

This is a retrospective cross-sectional study using programmatic data on NIKSHAY (a web-based case-based monitoring system under NTEP) collected routinely under the NTEP.

Study Area

Bengaluru city, Karnataka comprising 9 CBNAAT Sites (6 public & 3 private) within 22 Tuberculosis Units (TU), SDS -DR TB Centre and the National Reference Laboratory, National Tuberculosis Institute, Bengaluru (Culture and Drug Sensitivity Testing – C&DST) catering PMDT services under NTEP.

Study Population & Study Period

All the TB patients notified during the period 1st January 2017 to 31st December 2020 in Bengaluru city comprise the study population. The reasoning behind selection of the study period is that it is in concordance to the programmatic implementation of UDST following the newer diagnostic algorithms in the study area.

Sampling

The entire NIKSHAY data sets for the study period comprises the study sample. That includes all the notified TB cases from both public and private health care providers in the study area. Hence, no specific sampling method was adopted in determination of sample size.

Inclusion Criteria

- Patients of all age groups and all the genders registered and notified during the study period.
- All form of confirmed DR TB patients from Bengaluru city.

Exclusion Criteria

- Patients not residing in the study area.

Data Collection and Analysis

Requisite data for the study was collected from notification and PMDT modules available at the NIKSHAY portal through the office of the District Tuberculosis Officer, Bengaluru city and DR-TB Centre, SDS - TRC & RGICD Campus, Bengaluru.

Data analysis was conducted in Python (version 3.9.4) using appropriate statistical libraries. Data collected in the study was used to estimate the percentage of drug resistance in each year, to any drug, each drug either alone or in combination with other drugs. The percentage of resistant isolates from patients was calculated by dividing the number of resistant isolates in each of the categories by the total number of isolates tested for that drug or combination of drugs. Data expressed as absolute number with proportions with 95% confidence intervals. The chi square test for trend was used to assess percentage resistance by year of report at the 5% critical value. The ArcMap (version 10.8) of ArcGIS software system developed by Environmental Systems Research Institute (ESRI) was used to undertake the spatiotemporal analysis of DR TB patients in the study area.

Ethical Consideration

The study undertaken is purely a retrospective record-based study, based on the analysis of secondary data collected under the NTEP in Bengaluru city. The researcher did not have any direct interaction with the TB/DR TB patients and the study procedures do not pose any hazards, intervention/procedure and medications. Individual personal identification details and other relevant information pertaining to the study participants are confidential and not shared in the public domain. The study was ethically approved by the National Tuberculosis Institute - Institutional Ethics Committee (NTI-IEC), Bengaluru registered under Central Drug Standards Control Organisation (CDSCO) vide licence No. ECR/1194/Inst/KA/2019 on 16th September 2020.

RESULTS

A total of 37,984 TB cases were notified and initiated on treatment from 2017 to 2020. Among these overall notified cases, 24,058 (63.3%) were from public and 13,926 (36.7%) from private sectors. Out of the total TB cases, 24,343 (64.1%) cases were microbiologically confirmed and remaining 13,641 (35.9%) were clinically diagnosed TB cases. Of the microbiologically confirmed TB cases overall 23,654 (97.2%) were drug sensitive TB cases and 689 (2.8%) were diagnosed as DR TB cases having resistance to any first line anti TB drug. The mean age of the DR TB patients was observed as 36.7 years (95% CI: 22.3-51.1). Of the total 689 DR TB cases 434(63.0%) were male, 254(36.9%) were female and 01(0.1%) were transgender. About 686 (99.6%) were diagnosed at public health care settings and 03(0.4%) were diagnosed at the private health care settings. About 570 (82.7%) cases were pulmonary, 76 (11.0%) were extra pulmonary TB patients and site of TB disease was not recorded for 43 (6.2%) patients. The burden of DR TB was highest in the key population groups' i.e. urban slum dwellers (19.7%; 95% CI: 16.8-22.9), patients with diabetes mellitus (18.7%; 95% CI: 15.9-21.8), HIV co-infected (4.9%; 95% CI: 3.4-6.8), tobacco users (2.9%; 95% CI: 1.8-4.5) and history of contact with TB patients (1.5%; CI: 0.7-2.7). The detailed social, demographic and clinical profile of the study participants are presented in Table-1.

Out of the total DR TB cases, 412 (59.8%) cases were MDR RIF resistant, 268 (38.9%) were INH resistant, 66 (9.6%) were MDR and 8 (1.2%) were of XDR (MDR cases with additional resistance to Fluoroquinolone-FQ & Second line injectable –SLI) patients observed during the study period. The drug susceptibility profile among the study population by different study years are presented in Table-2. For estimating prevalence proportion of DR TB, the number of resistant isolates in each of the categories was divided by the total number of isolates tested for that drug or combination of drugs in the respective category. Out of the total 689 DR TB cases about 628 (91%) were microbiologically confirmed cases and the remaining 61 (9%) were clinically diagnosed. Therefore, for estimating the prevalence of DR TB only these microbiologically confirmed cases were considered. The overall prevalence of DR TB during the study years was estimated at 6.5% (95% CI: 6.0 - 7.0). Prevalence for DR TB for individual years was estimated at 4.4% (95% CI: 3.3–5.7), 4.7% (95% CI: 3.9-5.6), 6.4% (95% CI: 5.6-7.3), 8.8% (95% CI: 7.9-9.9) for the years 2017, 2018, 2019 and 2020 respectively.

The study finding highlights the increasing trends of DR TB in Bengaluru city from 4.4% to 8.8% ($p < 0.001$) out of the

microbiologically confirmed TB patients diagnosed during 2017 to 2020. The prevalence and trends of DR TB in Bengaluru city represented in the Table 3 & Figure-1. The spatiotemporal analysis undertaken in this study highlights the areas with aggregation of DR TB and MDR RR TB patients in Bengaluru city, the details of these hotspots are given in Table 4 & Table 5. The spatial-temporal distribution of these patients on Bengaluru city map is given in Figure-2.

Table 1: Social, Demographic, and clinical profile of DR TB patients initiated on treatment under NTEP during 2017 to 2020 in Bengaluru city, Karnataka

Characteristics	2017 (n & %)	2018 (n & %)	2019 (n & %)	2020 (n & %)	Total (n & %)
TOTAL NOTIFIED CASES	**8163**	**9313**	**11830**	**8678**	**37984**
Total notified in Public HCF	6421 (78.7%)	6699 (71.9%)	6467 (54.7%)	4471 (51.5%)	24058 (63.3%)
Total notified in Pvt HCF	1742 (21.3%)	2614 (28.1%)	5363 (45.3)	4207 (48.5%)	13926 (36.7%)
Total clinically diagnosed	2432 (29.8%)	3485 (37.4%)	4264 (36.0%)	3460 (39.9%)	13641 (35.9%)
Total microbiologically confirmed	5731 (70.2%)	5828 (62.6%)	7566 (64.0%	5218 (60.1%)	24343 (64.1%)
- Drug Sensitive TB	5661 (98.8%)	5693 (97.7%)	7346 (97.1%)	4954 (94.9%)	23654 (97.2%)
- Drug resistant TB	70 (1.2%)	135 (2.3%)	220 (2.9%)	264 (5.1%)	689 (2.8%)
Age (in years)					
0-14	2 (2.9%)	5 (3.7%)	2 (0.9%)	05 (1.9%)	14 (2.0%)
15-24	17 (24.3%)	27 (20.0%)	48 (21.8%)	69 (26.1%)	161 (23.4%)
25-34	13 (18.6%)	29 (21.5%)	47 (21.4%)	61 (23.1%)	150 (21.8%)
35-44	15 (21.4%)	31 (23.0)	50 (22.7%)	47 (17.8%)	143 (20.8%)
45-54	18 (25.7%)	22 (16.3%)	36 (16.4%)	54 (20.5%)	130 (18.9%)
55-64	03 (4.3%)	16 (11.9%)	30 (13.6%)	20 (7.6%)	69 (10.0%)
≥65	02 (2.9%)	05 (3.7%)	07 (3.2%)	08 (3.0%)	22 (3.2%)
Mean age	36.23 (SD 13.23)	37.4 (SD 15.17)	37.7 (SD 14.38)	35.56 (SD 14.38)	36.68 (SD 14.38)
Gender					
Male	46 (65.7%)	87 (64.4%)	152 (69.1%)	149 (56.4%)	434 (63.0%)
Female	23 (32.9%)	48 (35.6%)	68 (30.9%)	115 (43.6%)	254 (36.9%)
Transgender	01 (1.4%)	00	00	00	01 (0.1%)
Treatment care facility					
Public sector	70 (100%)	134 (99.3%)	218 (99.1%)	264 (100%)	686 (99.6%)
Private sector	00	01(0.7%)	02 (0.9%)	00	03 (0.4%)
Site of TB					
Pulmonary	39 (55.7%)	106 (78.5%)	199 (90.5%)	226 (85.6%)	570 (82.7%)
Extra pulmonary	03 (4.3%)	14 (10.4%)	21 (9.5%)	38 (14.4%)	76 (11.0%)
Not recorded	28 (40.0%)	15 (11.1%)	00	00	43 (6.2%)
Key population/Risk factors					
Diabetes mellitus	08 (11.4%)	29 (21.5%)	43 (19.5)	49 (18.6%)	129 (18.7%)
Tobacco/Smoking	02 (2.9%)	04 (3.0%)	05 (2.3%)	09 (3.4%)	20 (2.9%)
Urban slums	12 (17.1%)	34 (25.2%)	48 (21.8%)	42 (15.9%)	136 (19.7%)
Miner	0	1 (0.7%)	0	0	01 (0.1%)
Health care worker	0	0	02 (0.9%)	01 (0.4%)	03 (0.4%)
H/O contact with TB patient	0	03 (2.2%)	02 (0.9%)	05 (1.9%)	10 (1.5%)
HIV Status-Reactive	04 (5.7%)	06 (4.4%)	13 (5.9%)	11 (4.2%)	34 (4.9%)
ART status among HIV reactive					
Initiated on ART	02 (50%)	03 (50%)	13 (100%)		
Laboratory methods used among diagnosed DR TB cases					
Sputum smear (ZN & Fluorescent)	8 (11.4%)	21 (15.6%)	11 (5.0%)	10 (3.8%)	50 (7.3%)
Xpert MTB/Truenat	51 (72.9%)	91 (67.4%)	122 (55.5%)	118 (44.7%)	382 (55.4%)
Culture & DST	01 (1.4%)	02 (1.5%)	02 (0.9%)	03 (1.1%)	08 (1.2%)
LPA 1st line	09 (12.9%)	15 (11.1%)	74 (33.6%)	124 (47.0%)	222 (32.2%)
LPA 2nd line	00 (00%)	03 (2.2%)	09 (4.1%)	09 (3.4%)	21 (3.0%)
Other	01 (1.4%)	03 (2.2%)	02 (0.9%)	00	06 (0.9%)

Table 2: Drug susceptibility profile of the DR TB patients under NTEP during 2017 to 2020 in Bengaluru city, Karnataka

Drug susceptibility pattern	2017 (n & %)	2018 (n & %)	2019 (n & %)	2020(n & %)	Total (n & %)
Total microbiologically confirmed cases	5731 (70.2%)	5828 (62.6%)	7566 (64.0%)	5218 (60.1%)	24343 (64.1%)
Total drug Sensitive	5661 (98.8%)	5693 (97.7%)	7346 (97.1%)	4954 (94.9%)	23654 (97.2%)
Total drug resistant	70 (1.2%)	135 (2.3%)	220 (2.9%)	264 (5.1%)	689 (2.8%)
MDR RIF resistance	51 (72.9%)	102 (75.6%)	133 (60.5%)	126 (47.7%)	412 (59.8%)
INH resistance	03 (4.3%)	14 (10.4%)	95 (43.2%)	156 (59.1%)	268 (38.9%)
FQ resistance	00	08 (5.9%)	26 (11.8%)	19 (7.2%)	53 (7.7%)
SLI resistance	00	04 (2.9%)	04 (1.8%)	04 (1.5%)	12 (1.7%)
MDR (RIF+INH)	02 (2.9%)	04 (3.0%)	23 (10.5%)	37 (14.0%)	66 (9.6%)
XDR (MDR+FQ+SLI)	00	04 (3.0%)	02 (0.9%)	02 (0.8%)	08 (1.2%)

**actual % are out of respective years DR TB cases*

Table 3: Prevalence and trends of DR TB among TB patients in Bengaluru city, 2017-2020

Cases	2017-2020			2017			2018			2019			2020		
	n	P	CI	n	P	CI	n	P	CI	n	P	CI	n	P	CI
Total Case	37984			8163			9313			11830			8678		
Microbiologically confirmed cases	24343			5731			5828			7566			5218		
Drug Resistance, any	628	6.5	6.0 - 7.0	52	4.4	3.3 - 5.7	113	4.7	3.9 - 5.6	212	6.4	5.6 - 7.3	251	8.8	7.8 – 9.9
MDR RIF	412	4.2	3.8 – 4.6	51	4.3	3.2 – 5.6	102	4.3	3.5 – 5.1	133	4.0	3.4 – 4.8	126	4.4	3.7 – 5.2
XDR	08	1.9	0.8 – 3.8	00	00	00	04	3.9	1.1 – 9.7	02	1.5	0.2 - 5.3	02	1.6	0.2 – 5.6

P=Prevalence (%); CI= 95% confidence interval; Prevalence was estimated by dividing the no. of isolates in each category by total number of diagnostic tests offered in respective category; p=non-zero correlation of Cochran –Mentel Haenszel;

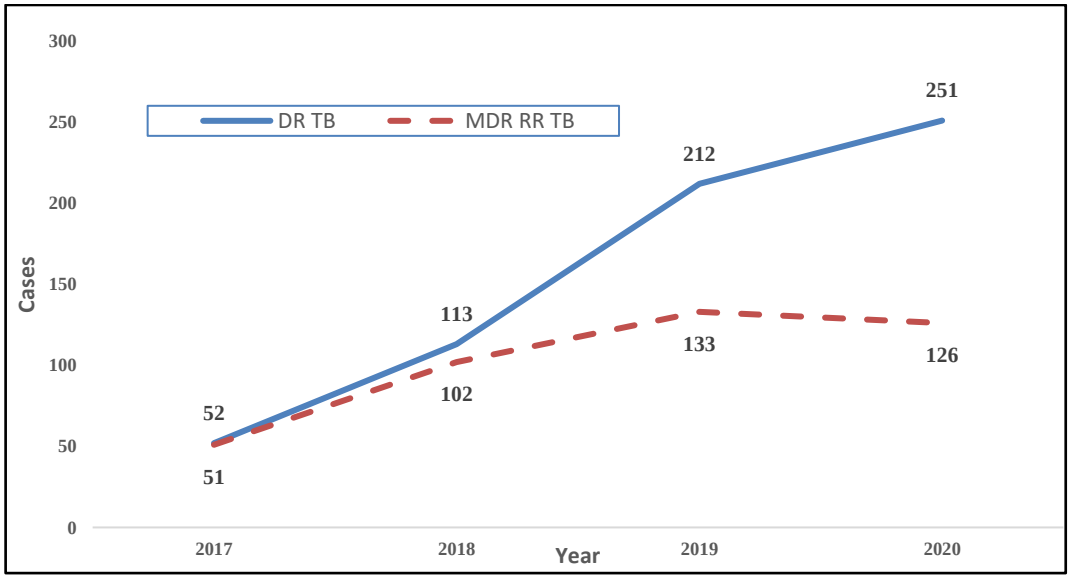


Fig 1: Trend of DR TB & MDR RR TB, Bengaluru City (2017 -2020)

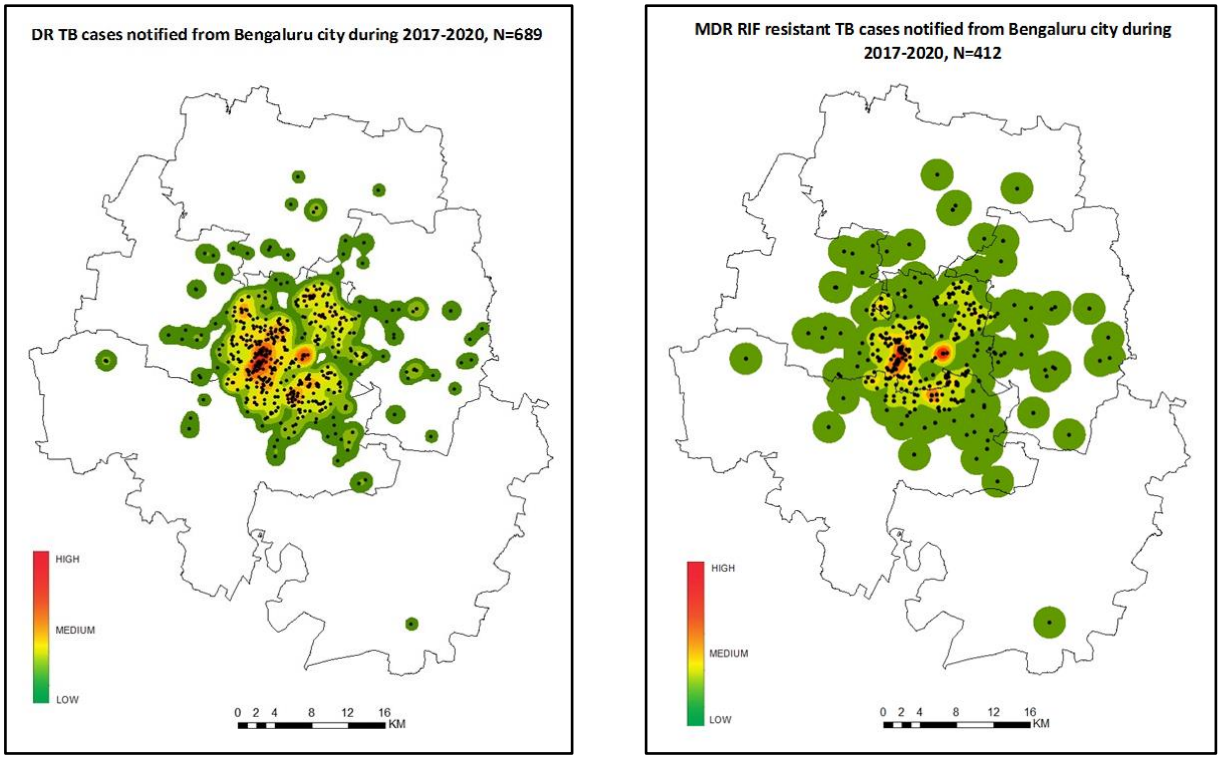
Table 4: Areas with higher DR TB patients clustering in Bengaluru city

2017	2018	2019	2020	2017-2020
Shanthala Nagar	Sampangirama Nagar	Rajajinagar	Srirampura	Shanthala Nagar
Nagarathpete	Nagarathpete	Basaveshwar Nagar	Prakash Nagar	Srinivas Nagar
Ashok Nagar	Shivaji Nagar	Vijaya Nagar	Basaveshwar Nagar	Ashok Nagar
Sampangirama Nagara	Ashok Nagar	Bapuji Nagar	Chamrajpet	Nagarathpete
Jayanagar	Chickpet	Chamrajpet	Vishhweshwarapura	Chamrajpet
			Shaman Nagar	Bapuji Nagar
				Manjunath Nagar
				Gopalapura
				Jagajeevanram Nagar

Table 5: Areas with higher MDR RIF resistant TB patients clustering in Bengaluru city

2017	2018	2019	2020	2017-2020
Hombegowda nagar	Ambedkar Veedhi	Bapujinagar	Giri Nagar	Guddadahalli
Jayanagar	Chickpet	Vijaya nagar	Avalahalli	Jagajeevanram Nagar
Tilak Nagar	Nagarathpete	Cholourpalya	Rajaji Nagar	Cholourpalya
Vijaya nagar		Binnipete	Azad Nagar	Gopalapura
		Srinagar	Brindavan Nagar	Keshava Nagar
		Brindavan Nagar	Venkatram nagar	Chamrajpet
				Ramchandraagrahara
				Jagajeevanram Nagar

Fig 2: The heat map showing spatiotemporal distribution of study population



DISCUSSION

The evolution of drug-resistant TB can be controlled by ensuring rapid and timely TB diagnosis, adequate infection control in TB treatment facilities, judicious and correct use of drugs for therapy, patient compliance to drug regimen and social awareness on TB control and drug regimen. However, the emergence of drug resistant tuberculosis has become a significant public health problem interfering in effective TB control programmes, additionally it also reflects on the effectiveness in management of drug-sensitive TB cases under the National TB control/elimination programme.[17] NTEP requires knowledge sharing and evidence on the effectiveness of the services rendered under PMDT to optimize policies, improve service quality and increase operational efficiency. The research studies on DR TB are very limited in the state of Karnataka. A few studies are published with regards to prevalence of DR TB from south coastal Karnataka;[18] airborne infection control (AIC) in DR TB Centres;[19] spatiotemporal analysis of DR TB in costal districts;[20] patient treatment pathways of MDR TB in coastal south India etc.[21] Thus, this study probably highlights the epidemiology of DR TB for the very first time in Bengaluru city.

In the present study out of 24,343 microbiologically confirmed TB cases; 23,654 (97.2%) of the cases were susceptible to the first line anti-TB drugs and 689 (2.8%) were resistant to at least one or more anti-TB drugs indicating the burden of drug resistant TB for the first line anti-TB drugs in Bengaluru city. Overall, the prevalence of DR TB in Bengaluru city was estimated as 6.5% (95% CI: 6.0-7.0) is considerably lower than the national estimate of 28% (CI 26.77–29.29%) as reported in the findings of National Drug Resistance Surveillance (2014–2016).[22] This might be attributable to under implementation of Universal Drug Susceptibility Testing (UDST) in the study area that was observed at 17.7% (2017), 43.3% (2018), 56.3% (2019) and 63.4% (2020). Similarly, prevalence of MDR RIF resistance TB was estimated at 4.2% (95%CI: 3.8-4.6) against the national estimate of 6.19% (5.5-6.9) that is higher than the WHO estimated proportions of TB cases with MDR/RR TB of 2.8% (2.3-3.5) in India.[2,22]

The magnitude of resistance to any anti-TB drug in the present study could be explained through difference in the characteristic of study participants. Male patients (63%) are more vulnerable than females (36.9%), patients in the middle age group are at higher risk (mean age 36.68 years & SD 14.38 years), key population such as urban slum dwellers (19.7%), diabetes mellitus (18.7%), HIV coinfection (4.9%) etc. are more vulnerable to get drug resistance to the anti-TB drugs. Study conducted by Amit M Shah et al also reported middle age groups (21–30 years & 31–40

years) were most commonly affected with MDR-TB.[23] Therefore, all above factors have been recognised as the possible causes for increased risk of acquiring MDR-TB by various research studies.[24-26]

The trend in drug resistance against all first line drugs demonstrates an increase in the study area, this might be due to the implementation of improved case finding and universal culture and DST rolled out during the year 2017 under PMDT guidelines. However, under-coverage of UDST among the notified cases may result in missing DR TB cases and consequently in under estimation of DR TB burden in the study area. Additionally, the COVID-19 pandemic influenced grossly on the TB care services during the year 2020 resulting the under-case notifications. Due to under implementation of UDST we were not able to calculate the mono RIF & mono INH resistant, as all the cases were not subjected to both CBNAAT/TreuNat & First Line Probe Assay (FLPA). However, an effort was put in to provide their actual percentage in the study group. Notably, prevalence of MDR RIF resistant is found within 5% during the study years. However, there is a significant increase in the proportions of INH resistance among the isolates subjected to the first-line Line Probe Assay (LPA) and DST, which may be considered as an alarming sign and indicates further transmission of resistant strains in the community. In addition, in the study we could not do subgroup analysis to see the resistance pattern among previously treated and newly diagnosed TB patients, due to the limitation, as in the programmatic data all the DR TB cases as termed as PMDT cases. Study conducted by Padda P et al highlighted that 25% of TB/HIV coordinators felt that filling the reporting form was time consuming and 16.5% entries in the DR TB register were found missing.[27] This highlight the lacunae in terms of complete data recording and reporting in NIKSHAY under the programmatic conditions, that need to be addressed through proper sensitisations/trainings of the programme personals aiming towards minimising the data entry errors and assuring its completeness in NIKSHAY portal.

It is proven fact that poor treatment practices raise drug resistance among the patients. Areas with a poor TB control tend to have higher rates of DR-TB. It has been acknowledged that UDST & good treatment is the prerequisite towards the prevention of emergence of drug resistance. Prevention of emergence of MDR-TB in the community is more imperious rather than its treatment. It is impossible to tackle the problem of DR-TB through treatment alone; treating each MDR-TB case costs more than 20 times the cost of a drug-susceptible TB case, therefore, basic TB diagnostic and treatment services would be prioritized and implemented effectively as per the programmatic guidelines.[28] Thus, multipronged strategy focusing on End TB strategy by improving diagnostic capacity, guaranteeing high-quality treatment and preventing transmission will be central to meeting the challenge of DR-TB in India.[29]

Implication of this study is for programme managers and researchers to undertake similar future studies by using the available programmatic data at a wider platform such as state, zonal and national levels to monitor the epidemiological trends of DR TB. In addition, similar studies will be helpful to the programme managers/researchers for periodically monitoring the impact of PMDT activities in their respective areas of operations to assess the progress made towards the goals of End TB Strategy. The study highlights the need for upfront UDST to diagnose early and notify the missing cases of DR TB in the study area to further prevent the transmission of disease. The TB Preventive Therapy (TPT) may be offered to all the household contacts of all the DR TB cases as per the programmatic guidelines. The important implication of this study is the DR TB hotspots identified by the geospatial analysis in the Bengaluru city further warranting the need of intensified Active Case Finding (ACF) in the identified clusters.

LIMITATION OF THE STUDY

The research study designed is limited on available retrospective data collected routinely under the programmatic conditions.

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REFERENCES

1. Central TB Division. TB India - Revised National Tuberculosis Control Programme. Annual Status Report. 2019.
2. World Health Organization, Geneva. Global tuberculosis report: Tuberculosis profile - India. 2020.
3. Sharma N, Basu S and Chopra KK. Achieving TB elimination in India: The role of latent TB management. Indian J Tuberc. 2019;66(1):30-33.
4. World Health Organization, Geneva. Global Tuberculosis Report: Tuberculosis profile - India. 2021.
5. Scroll – Medical Care. In India, over 56% of multidrug-resistant TB cases remains undetected and over 64% untreated. 2019. Source: Available from: https://Scroll.in/article/print/941815. Accessed May, 2021.
6. Central TB Division. TB India - Revised National Tuberculosis Control Programme. Annual Status Report. 2016.
7. Ministry of Health and Family Welfare, New Delhi. National Tuberculosis Elimination Programme. National Strategic Plan to End Tuberculosis in India. 2020.
8. World Health Organisation, Geneva. Global Tuberculosis Report: Tuberculosis profile - India. 2019.
9. WHO. Engaging private health care providers in TB care and prevention: a landscape analysis. World Health Organization. 2018. Available from: https://apps.who.int/iris/handle/10665/333886. Access June, 2021.
10. World Bank Group. India: Program towards Elimination of Tuberculosis (P167523). Technical Assessment Report. 2018. Available from: https://documents1.worldbank.org/curated/en/150891551214323148/pdf/Final-Technical-Assessment-Program-Towards-Elimination-of-Tuberculosis-P167523.pdf. Accessed June, 2020

11. Shah AM, Shah RB and Dave PN. Factors contributing to development of multidrug-resistant tuberculosis. Natl J Physiol Pharm Pharmacol. 2018;8(10): 1463-1469.
12. Janmeja AK, Deepak A and Dhillon R. Analysis of treatment outcome in multi-drug resistant tuberculosis patients treated under programmatic conditions. Int J Res Med Sci. 2017;5:2401-2405.
13. Directorate of Census Operations Karnataka. District Census Handbook – Bengaluru. Census of India. 2011; Series 30 (part XIIA): 31.
14. TOG-Chapter 4-Treatment of TB: Central TB Division [Internet]. Accessed June, 2020. Available from: https://tbcindia.gov.in/index1.php?sublinkid=4611&level=3&lid=3221&lang=1 .
15. Government of Karnataka. National Health Mission. Health and Family welfare services. ndcp_cd_rntcp [Internet]. Accessed on June, 2020. Available from: karunadu.karnataka.gov.in/hfw/nhm/pages/ndcp_cd_rntcp.aspx .
16. Central TB Division, New Delhi, India. Technical and operational guidelines for tuberculosis control in India. 2016. https://www.tbcindia.gov.in/index1.php?lang=1&level=2&sublinkid=4573&lid=3177
17. Pinto L, Menzies D. Treatment of Drug Resistant Tuberculosis. Infect Drug Resist. 2011;4:129-135.
18. Rao P, Chawla K, Shenoy VP, et al. Study of drug resistance in pulmonary tuberculosis cases in south coastal Karnataka. Journal of Epidemiology and Global Health. 2015;5:275–281.
19. Akshaya KB, Shewade HD, Aslesh OP, et al. "Who has to do it at the end of the day? Programme officials or hospital authorities?" Airborne infection control at drug resistant tuberculosis (DR-TB) centres of Karnataka, India: a mixed-methods study. Antimicrobial Resistance and Infection Control. 2017;6:111.
20. Poojar B, Shenoy KA, Naik PR, et al. Spatiotemporal analysis of drug-resistant TB patients registered in selected districts of Karnataka, South India: a cross-sectional study. Tropical Medicine and Health. 2020;48:15.
21. Rathi P, Shringarpure K, Unnikrishnan B, et al. Patient treatment pathways of multidrug-resistant tuberculosis cases in coastal South India: Road to a drug resistant tuberculosis center. F1000Research. 2020;8:498.
22. Ministry of Health and Family Welfare, Government of India. Report of the first national anti-tuberculosis drug resistance survey: India 2014–16. 2018. Accessed May 2020.
Available from: https://tbcindia.gov.in/showfile.php?lid=3315 .
23. Shah AM, Shah RB, Dave PN. Factors contributing to development of multidrug-resistant tuberculosis. Natl J Physiol Pharm Pharmacol. 2018;8(10): 1463-1469.
24. McCray E, Onorato IM. The interaction of human immunodeficiency virus and multidrug resistant Mycobacterium tuberculosis. Multidrug-Resistant Tuberculosis. Kluwer Academic Publishers; 2000:45-57.
25. Frieden TR, Sterling T, Pablos-Mendez A, et al. The emergence of drug-resistant tuberculosis in New York city. N Engl J Med. 1993;328:521-526.
26. Edlin BR, Tokars JI, Grieco MH, et al. An outbreak of multidrug- resistant tuberculosis among hospitalized patients with the acquired immunodeficiency syndrome. N Engl J Med. 1992;326:1514-1521.
27. Padda P, Singla N, Sarin R. Surveillance, Evaluation of Programmatic Management of Drug Resistant Tuberculosis (PMDT) at DR-TB Centre, NITRD, New Delhi. Indian J Comm Health. 2018;30(1):76-81.
28. Kumar A, Singh AK, Upadhyay V, et al. Epidemiology of multi-drug-resistant tuberculosis in Northern India. Biomed Biotechnol Res J. 2018;2(2):112-121.
29. Chatterjee S, Poonawala H, Jain Y. Drug-resistant tuberculosis: is India ready for the challenge? BMJ Glob Health. 2018;3:e000971

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