

Original Research Articles

Management of Tuberculosis including Drug-Resistant TB in Private Sector of Mumbai, India

ABSTRACT

Objectives: To find out practices in Mumbai's private sector regarding management of TB in new patients including those when such patients do not respond to treatment and to find out practices related to diagnosis and treatment of drug-resistance.

Methods: A total of 42 chest physicians (CP), 51 post-graduates in general medicine (MD), 70 allopathic graduates (AP) and 33 ayurvedic/homeopathic physicians (ISM) participated in this cross sectional study. A pre-designed pilot tested questionnaire was used to record practices of physicians which were compared with International standards for Tuberculosis care (ISTC).

Results: Most physicians across all groups reported use of sputum microscopy for diagnosis. ISTC recommended regimens were prescribed by 29% CP, 31% MD, 9% AP and 9% ISM practitioners. Monitoring of treatment by sputum smear microscopy was reported by 95%, 78%, 46% and 57% respectively. 36% CP, 58% MD, 40% AP and 53% ISM reported suspecting drug resistance among non-responders at three months of treatment. 43% CP, 26% MD, 27% AP and 18% ISM practitioners prescribed retreatment regimen without investigating for drug-resistance among patients not responding to first regimen. 50% CP and 60% MD prescribed standardised regimens for treatment of multidrug-resistant TB and regimens prescribed by 25% CP and 9% MD were in line with ISTC. The specialists (CP and MD) were significantly more likely than family physicians to adhere to ISTC recommendations related to diagnosis, treatment and monitoring of new TB cases.

Conclusions: Management of TB among new patients was deviating from ISTC recommendations more so among AP and ISM than in CP and MD groups. There is delay in suspecting drug-resistance in private sector. Majority of regimens offered for treating multidrug-resistant TB are not individualised and most are inadequate. There is need to train physicians in standards for TB care in India (STCI).

Keywords: Tuberculosis, Drug-resistance, Private practitioners, Clinical practices

1. INTRODUCTION

Tuberculosis (TB) continues to be among leading causes of mortality with 1.3 million deaths in 2012 alone (1). India is among 22 high TB burden countries and accounts for nearly one fourth (2.2 million) of global new cases (2). In absence of effective vaccine to prevent infection and/or disease, TB control relies mainly on early detection and prompt treatment of disease. Appropriate treatment can cure patients and thereby reduce transmission of infection to others. Many countries including India have adopted WHO recommended Direct Observation of Treatment with Short course chemotherapy (DOTS) strategy. The DOTS strategy based public health programmes have expanded access to treatment with evidence based standardised regimens (3). However, majority of patients in most high burden countries access treatment from private sector (4). In India, more than 70% of illness spells are treated in private sector (5). Public Private Mix (PPM) projects were initiated in India to involve private practitioners in government's DOTS based Revised National TB Control Programme (RNTCP). But these projects have met with limited success; only 5% of the total sputum positive case detection under RNTCP in the intensified urban PPM areas is

contributed by private practitioners (6). Majority of patients approaching private practitioners are not referred to RNTCP and are being managed in private sector itself (7).

Researchers have studied TB management practices in private sector in the past. In the first study of its kind conducted two and half decades ago, Uplekar and Shepherd highlighted the inappropriate practices of general practitioners related to management of TB in Mumbai, India (8). Since then other studies from India have consistently found large variance in regimens prescribed many of which were inappropriate (9,10,11,12,13). Systematic reviews of published literature from various countries have highlighted lack of knowledge regarding appropriate management of TB and irrational use of anti-tubercular drugs (14,15).

The management practices related to TB have reached grave significance today due to changing epidemiology of *Mycobacterium tuberculosis*. It is well known that natural microorganisms possess genes that can resist action of antibiotics on them and gene exchange among microorganisms can propagate drug resistance (16). With respect to TB, this natural process is accentuated due to irrational use of anti-tubercular drugs. Inadequate treatment regimens prescribed by medical practitioners and poor compliance to treatment have resulted in selection of resistant mutants of TB bacilli (17). This has created epidemiological shift where drug sensitive TB is being replaced by drug-resistant (DR) forms of TB including multidrug-resistant (MDR) and extensively drug-resistant (XDR) (18).

India is estimated to have about 99,000 cases of DR-TB (19). Out of these, only about 20,000 patients were provided treatment for MDR TB under RNTCP in 2013 (6). Many of the remaining patients are likely to be accessing treatment in private sector. There is lack of literature on their management in private sector. Data from city of Mumbai reflects similar situation. The city has high burden of TB and drug-resistant TB (20,21). Recent mortality data from Mumbai revealed that although 7127 TB deaths were registered in Mumbai as per vital registration records, only 1393 were reported by RNTCP (22). This provides evidence that many TB patients are still out of reach of RNTCP and continue to take treatment from private healthcare providers in Mumbai.

Almost all of the published literature on TB care in India's private sector is about management of new TB cases. There is relative lack of literature related to management of DR-TB. DR-TB is a laboratory diagnosis and it is not possible to differentiate between drug susceptible and resistant forms clinically. Also, drug susceptible forms may be replaced by drug resistant forms due to inadequate treatment. Therefore, DR-TB needs to be suspected and investigated for patients not responding to treatment. There is no data available from private sector on when and how is DR-TB suspected, how are they being diagnosed and what treatment is offered to them. Hence, it was pertinent to study not just the new patients but also what practices are followed for patients not responding to treatment and practices related to diagnosis and treatment of DR-TB.

2. MATERIAL AND METHODS

Study Settings

In Mumbai, TB among adults is treated by a range of private providers including medical graduates and postgraduates. The medical graduates have been referred to as family physicians and postgraduates as specialist in this paper. Postgraduates treating TB chiefly include those with masters in chest medicine (CP) and general medicine (MD). The family physicians (FP) include those from allopathy stream (AP) as well as those from other systems of medicine including homeopathy, ayurveda and unani. The state government of Maharashtra has made regulations that allow practitioners with graduation in ayurveda and homeopathy to prescribe allopathic medications including anti-tubercular drugs.

Study design

A cross sectional study design was used where healthcare providers were approached and were asked to report their practices with respect to management of TB. Study proposal was approved by Board of Studies, School of Health Systems Studies, Tata Institute of Social Sciences, Mumbai.

Selection of study respondents

85 The study participants included specialists as well as family physicians. Among specialists, only
 86 the two commonest groups, namely chest physicians (CP) and post-graduates in general medicine
 87 (MD) were included. Among family physicians only those trained in allopathy (AP), homeopathy
 88 and ayurveda were included; the last two jointly referred to as ISM practitioners in this paper.
 89 Qualified medical practitioners from other systems of medicine and unqualified medical
 90 practitioners were not included in this study as the government regulations prohibit them from
 91 prescribing anti-TB drugs. Providing medical care to TB patients and practising in Mumbai metro-
 92 city were inclusion criteria. From feasibility point of view, sample size was planned as 50 CP, 50
 93 GP and 100 FP. For chest physician (CP) group, list was prepared by referring to directory of
 94 Indian Association for Bronchology and Indian Chest Society, visits to major private hospitals and
 95 polyclinics by research officers. Thus, a list of chest physicians was prepared and attempts were
 96 made to contact them and invite them to participate in the study. The chest physicians who
 97 participated were requested to suggest names of fellow CP and thus snowball technique was
 98 employed to recruit more participants. List for MD group was also prepared by visits to major
 99 private hospitals and polyclinics by research officers; these practitioners were invited to participate
 100 in the study as well as suggest other practitioners. For FP, three wards of Mumbai were chosen
 101 purposively, two with middle and higher income groups (A, K/West) and one with low income
 102 groups (M/East). These wards were further divided into localities and physicians practicing in two
 103 localities from each ward were invited to participate in the study.

104 Assessment of management practices

105

106 **Developing operational definitions**

107 Many guidelines exist for tuberculosis diagnosis, treatment, and control globally. These include the
 108 guidelines for treatment of tuberculosis from WHO (4th Ed.), RNTCP guidelines of India, the
 109 International Standards for Tuberculosis Care (ISTC) and the Standards for Tuberculosis Care in
 110 India (STCI) (23,24,25,26). The first two are more applicable to national health programme that
 111 presume it to be the end provider. The ISTC and STCI guidelines are more relevant for the private
 112 sector that manages TB in its own setting. STCI guidelines were framed only after completion of
 113 the present study; hence ISTC guidelines have been used for assessing management practices.
 114 International Standards for Tuberculosis Care (ISTC), 2009 has laid down standards for diagnosis
 115 and treatment of TB (23). For the purpose of this study, five ISTC standards were referred to
 116 (Table 1). Table 1 also shows respective questions or items developed to measure TB
 117 management practices. The study tool was revised after pre-testing it with five family physicians
 118 and three specialists.

119

120 **Table 1: International standards for Tuberculosis Care (2009) and items developed to**
 121 **assess management practices in private sector**

122

International Standards for Tuberculosis Care, 2009	Relevant item/s in the questionnaire
Standard 2: All patients suspected of having pulmonary tuberculosis should have at least two sputum specimens submitted for microscopic examination in a quality-assured laboratory.	• How do you diagnose pulmonary TB? List investigations used. • Importance of sputum microscopy compared with other tests
Standard 8: The initial phase should consist of two months of isoniazid (INH), rifampicin (RIF), pyrazinamide (PZA), and ethambutol (EMB). The continuation phase should consist of isoniazid and rifampicin given for four months.	• Write regimen (s) you prescribe including phases, combinations of drugs and duration of treatment for new pulmonary TB patients
Standard 10: Response to therapy in patients with pulmonary tuberculosis should be monitored by follow-up sputum microscopy at the time of completion of the initial phase of treatment (two months).	• How do you monitor progress of treatment in a new patient? List the investigations and mention timing of each

Standard 11: Patients who remain sputum smear-positive at completion of 3 months of treatment should always be assessed for drug resistance by culture and testing for susceptibility/resistance to at least isoniazid and rifampicin should be performed promptly	• Timing of suspecting DR-TB • Regimen prescribed when patient is not responding to treatment (before investigating for DR-TB) • Method for diagnosing MDR-TB
Standard 12: For patients with MDR-TB, the regimen chosen may be standardized or based on suspected or confirmed drug susceptibility patterns. At least four drugs to which the organisms are known or presumed to be susceptible, including an injectable agent, should be used and treatment should be given for at least 18–24 months beyond culture conversion.	• Type of regimen prescribed (standardised or based on drug susceptibility pattern) • Regimen prescribed for MDR-TB including phases, combinations of drugs and duration of treatment • Duration of treatment

MDR-TB regimens were classified as standardised, empiric and individualised after review of ISTC and WHO guidelines (23,24). A regimen was termed 'standardised' if the practitioner prescribed single regimen to all DR-TB patients. A regimen was termed 'empiric' if the practitioner initiated regimen without waiting for results of susceptibility testing based on history of drug used by patient. A regimen was termed 'individualised' if it was based on the results of susceptibility testing to second line drugs.

Data collection and analysis

Three research officers were recruited and oriented in basic aspects of TB infection, RNTCP and the International Standards for TB Care (ISTC). After administering informed consent, practitioners willing to participate were given pre-designed, pilot tested questionnaires. Data collection was completed over six month period from August 2011 to February 2012. Data was entered in Microsoft Excel version 14.0.0 and analysis involved calculation of frequencies and percentages of practices for variables mentioned above. For comparing TB management practices, proportions of practitioners following ISTC recommendations were compared across physician groups. For this comparison, specialists were considered as one group and family physicians were considered as other group and χ^2 test was employed. With respect to ISTC standard 12, no comparison was attempted due to smaller sample.

Ethical considerations

Ethical principles of 'Declaration of Helsinki' were followed for the study. Informed consent process specified confidentiality of respondents' identity and written consent was obtained. The data from the private practitioners was kept anonymous and confidential and information pertaining to individual patients was not collected. Data entered in excel file did not bear personal identifiers. No incentives were offered for participation in the study.

3. RESULTS

A total of 307 practitioners including 178 FP, 59 CP and 70 MD were approached. Of these, 21 reported that they do not treat TB and 87 refused to participate. Thus, 199 practitioners (106 FP, 42 CP and 51 MD) participated in the study. Only one-fourth of the family physicians and half of the specialists were formally trained/ sensitised in RNTCP.

Diagnosis of new pulmonary TB

The physicians reported use of various tests, either alone or in combination, to arrive at diagnosis of pulmonary tuberculosis. Among the diagnostic tests, x-ray was reported by all practitioners except three family physicians. Almost all specialists (CP and MD) were advising sputum smear microscopy for diagnosis of pulmonary TB. Eight (11%) AP and 7 (19%) ISM practitioners were not relying on sputum smears test for diagnosis. The specialists were more likely to use sputum smear microscopy than family physicians ($\chi^2 = 5.92$, $p = .015$). 168 practitioners responded to question regarding importance accorded to sputum smear microscopy. Table 1 show that almost all CP and majority of GP reported reliance on sputum smear microscopy. But majority of the family physicians accorded less importance to sputum smear microscopy than other tests. Two (4.8%) CP, 2 (3.9%) MD, 9 (12.9%) AP and 2 (5.6%) ISM reported using immune-globulins for diagnosis of TB (not shown in table).

Table 2: Sputum-smear microscopy in diagnosis of pulmonary TB – practices and opinions across physician groups^{\$}

Use of sputum smear microscopy for diagnosis of pulmonary TB	Chest Physicians (n = 42)	Post-graduates in general medicine (n = 51)	Family physicians (allopathic) (n = 70)	Family physicians (ISM) [#] (n = 36)
	No. (%)	No. (%)	No. (%)	No. (%)
Advise sputum smear microscopy*	41 (98)	49 (96)	62 (89)	29 (81)
Importance of sputum smear microscopy in diagnosis of pulmonary	n = 33	n = 47	n = 62	n = 26
Most important test	18 (54.5)	18 (39.1)	19 (30.6)	3 (11.5)
Equally important to other tests	11 (33.3)	13 (27.7)	2 (3.2)	7 (26.9)
Less important than other tests	1 (3.0)	9 (19.1)	10 (16.1)	4 (15.4)
Not important at all	3 (9.1)	7 (14.9)	31 (50.0)	12 (46.2)

^{\$}Only 168 responded about relative importance of sputum smear microscopy, [#]ISM: homeopathic and ayurvedic practitioners, * As per ISTC standard 2, $\chi^2 = 5.92$, $p = .015$

Treatment of new pulmonary TB

Data on drug combinations, duration and frequency of treatment regimen offered to new TB patients was available from 184 practitioners. A total of 84 different types of treatment regimens were being prescribed by these physicians. Table 3 shows regimens prescribed by study respondent. It starts with ISTC recommended regimen followed by other regimens. Other regimens were broadly classified into three categories. First category included regimens with less than four drugs or less duration of treatment than ISTC recommendation. Second category included four drugs recommended in ISTC but for duration longer than that of the guidelines. Third category included regimens with other drugs.

Among chest physicians, 19 (50%) were prescribing ISTC recommended drugs but for longer duration. Prescriptions of 11 (28.9%) CP was exactly like ISTC. While only 1 (2.6%) CP was prescribing a regimen with less drugs, 7 (18.4%) had drugs other than ISTC recommended as first line of treatment. Practices of MD were almost similar with 25 (51%) reported prescribing ISTC recommended regimens for longer duration and 15 (30.6%) adhering to ISTC recommendations. Six (12.2%) MD were prescribing less drugs and 3 (6.1%) were prescribing other drugs.

Nearly three fourths of AP (47, 73.4%) were treating patients for longer duration, 8 (12.5%) were prescribing less drugs and 3 (4.7%) were prescribing other drugs. Only 6 (9.4%) AP reported prescribing ISTC recommended regimen. Similar to AP, very few ISM practitioners (3, 9.1%) were prescribing ISTC regimen. Among ISM group, 13 (39.4%) were prescribing longer duration of treatment. This group was more often prescribing fewer drugs (10, 30.3%) and other drugs (7, 21.2%) than other groups. Specialists were more likely to use ISTC regimen than family physicians ($\chi^2 = 11.34$, $p < .001$).

Table 3: Treatment regimens prescribed across physician groups for new pulmonary TB patients

Regimens prescribed	Chest Physicians (n=38)	Post-graduates in general medicine (n = 49)	Family physicians (allopathic) (n=64)	Family physicians (ISM) # (n=33)
	No. (%)	No. (%)	No. (%)	No. (%)
a. Regimen as per International Standards for tuberculosis care (2HRZE + 4HR)*	11 (28.9)	15 (30.6)	6 (9.4)	3 (9.1)
b. Regimens with less than four drugs or drugs for less duration than ISTC recommendations	1 (2.6)	6 (12.2)	8 (12.5)	10 (30.3)
i) R < 6 months	0 (0.0)	1 (2.0)	5 (7.8)	6 (18.2)
ii) Regimen without Z	1 (2.6)	5 (10.2)	2 (3.1)	3 (9.1)
iii) Regimen without E	0 (0.0)	0 (0.0)	1 (1.6)	0 (0.0)
iv) H < 6 months	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.0)
c. Regimens with same drugs but for longer duration than recommended in ISTC	19 (50.0)	25 (51.0)	47 (73.4)	13 (39.4)
i) 2HRZE + 4HRE	9 (23.7)	11 (22.4)	11 (17.2)	2 (6.1)
ii) Z > 2 months	2 (5.3)	3 (6.1)	13 (20.3)	3 (9.1)
iii) 2HRZE + 6HR	0 (0.0)	3 (6.1)	3 (4.7)	1 (3.0)
iv) 2HRZE + 6HRE	3 (7.9)	2 (4.1)	1 (1.6)	0 (0.0)
v) Total duration > 8 months	5 (13.2)	6 (12.2)	19 (28.1)	7 (21.2)
d. Regimens with drugs different than ISTC recommendations	7 (18.4)	3 (6.1)	3 (4.7)	7 (21.2)
i) Use of second line drugs	4 (10.5)	1 (2.0)	1 (1.6)	4 (12.1)
ii) Five drug regimens (SHRZE)	3 (7.9)	2 (4.1)	2 (3.1)	3 (9.1)

H – Isoniazide, R – Rifampicin, Z – Pyrazinamide, E – Ethambutol, S – Streptomycin, #ISM: homeopathic and ayurvedic practitioners,

* As per ISTC standard 8, $\chi^2 = 11.34$, $p < .001$

Monitoring of treatment

Similar to diagnosis, one or more tests were employed by the practitioners in addition to clinical examination for monitoring success of TB treatment. 40 (95.2%) CP, 40 (78.4%) MD, 33 (46.4%) AP and 20 (56.8%) ISM used sputum microscopy for monitoring response to treatment (Table 4). Only CP group had sputum smear microscopy as commonest test for monitoring patient response. In all other groups, x-ray was most commonly reported test for monitoring response. Specialists were more likely to use sputum smear microscopy than family physicians ($\chi^2 = 27.4$, $p < .001$).

Table 4: Monitoring treatment among new pulmonary TB patients across physician groups

Tests used for monitoring response to TB treatment	Chest Physicians (n=42)	Post-graduates in general medicine (n = 51)	Family physicians (allopathic) (n=70)	Family physicians (ISM) [#] (n=36)
	No. (%)	No. (%)	No. (%)	No. (%)
Sputum smear microscopy*	40 (95.2)	40 (78.4)	33 (46.4)	20 (56.8)
X-ray chest	38 (90.5)	45 (88.2)	64 (91.3)	30 (83.8)
Complete Blood Count	20 (47.6)	23 (45.1)	32 (45.7)	23 (62.2)
Erythrocyte Sedimentation	19 (45.2)	23 (45.1)	49 (69.6)	26 (73.0)
Montoux test	0 (0.0)	3 (5.9)	4 (5.8)	6 (16.2)
Other tests	4 (9.5)	3 (5.9)	5 (7.2)	3 (8.1)

* as per ISTC standard 10, #ISM: homeopathic and ayurvedic practitioners, $\chi^2 = 27.4$, $p < .001$

Action taken for patient not responding to first regimen

A total of 40 FP (23 AP and 17 ISM) and one MD did not specify duration of therapy after which they would term a patient as non-responder and suspect drug resistance. Data from remaining physicians is presented in Table 5 which highlights delay in suspecting drug resistance. Only 15 (35.7%) CP, 29 (58.0%) MD, 19 (40.4%) AP and 10 (52.6%) ISM practitioners suspected drug resistance for patients not responding to three months of therapy. There was no statistical difference between delay in diagnosis between the specialists and the family physicians ($\chi^2 = 0.10$, $p = .75$).

Table 5: Delay in suspecting drug resistance by physicians in private sector, Mumbai

Time of suspecting drug resistance	Chest Physicians (n=42)	Post-graduates in general medicine (n = 50)	Family physicians (allopathic) (n=47)	Family physicians (ISM) [#] (n=19)
	No. (%)	No. (%)	No. (%)	No. (%)
No delay: Non-response at end of three months of first regimen*	15 (35.7)	29 (58.0)	19 (40.4)	10 (52.6)
Delay	27 (64.3)	21 (42.0)	28 (59.6)	9 (47.4)
i) Non-response at end of first regimen	21 (50.0)	16 (32.0)	21 (44.7)	5 (26.3)
ii) After second/third regimen	6 (14.3)	5 (10.0)	7 (14.9)	4 (21.1)

#ISM: homeopathic and ayurvedic practitioners, * As per ISTC standard 11, $\chi^2 = 0.10$, $p = .75$

Retreatment regimens prescribed for patient not responding to first regimen

A total of 18 (42.9%) CP, 13 (26.0%) MD, 19 (27.1%) AP and 6 (18.2%) ISM practitioners reported prescribing retreatment regimens without investigating for presence of drug resistance (Table 6). Most of these retreatment regimens included addition of single drug to failing regimen; streptomycin was most common choice followed by a fluoroquinolone for the additional drug. Only 11 physicians were adding two new drugs to retreatment regimens. However, none of these regimens had injectable drug for six months and total duration of treatment was less than 18 months. Majority of CP (24, 57.1%) and MD (33, 66.0%) investigated for presence of drug

resistance and determined regimen on results of such tests. Majority of AP (50, 71.4%) and ISM (27, 81.8%) practitioners reported referring patients to MD or CP if drug resistance was proven.

Table 6: Re-treatment regimens prescribed by physicians in private sector, Mumbai

Re-treatment regimen	Chest Physicians (n=42)	Post-graduates in general medicine (n = 50)	Family physicians (allopathic) (n=70)	Family physicians (ISM) # (n=33)
	No. (%)	No. (%)	No. (%)	No. (%)
Retreatment regimen offered without drug sensitivity test	18 (42.9)	13 (26.0)	19 (27.1)	6 (18.2)
a. Regimen with HRZE only	1 (2.4)	0 (0.0)	4 (5.7)	0 (0.0)
b. Regimen with one drug added	14 (33.3)	10 (20.0)	10 (14.3)	4 (12.1)
i) Fluroquinolone	1 (2.4)	3 (6.0)	3 (4.3)	1 (3.0)
ii) Streptomycin	12 (28.6)	7 (14.0)	3 (4.3)	2 (6.1)
iii) Kanamycin/ capreomycin	1 (2.4)	0 (0.0)	2 (2.9)	1 (3.0)
iv) Para Amino Salicyclic acid	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)
c. Regimen with addition of two new drugs	2 (4.8)	3 (6.0)	4 (5.7)	2 (6.1)
i) Injectable drug < 6 months	1 (2.4)	3 (6.0)	3 (4.3)	1 (3.0)
ii) Injectable drug for 6 months or more but total duration < 18 months	1 (2.4)	0 (0.0)	1 (1.4)	1 (3.0)
d. Details not sufficient	1 (2.4)	0 (0.0)	1 (1.4)	0 (0.0)
Retreatment regimen offered after and based on drug sensitivity test	24 (57.1)	33 (66.0)	1 (1.4)	0 (0.0)
Referred to other practitioners	0 (0.0)	4 (8.0)	50 (71.4)	27 (81.8)

#ISM: homeopathic and ayurvedic practitioners

Diagnosis and treatment of MDR-TB

A total of 84 specialists provided details of referral to laboratories for diagnosis of drug-resistance. Out of these 84, 48 (57.1%) were referring patients exclusively to RNTCP accredited laboratories, 19 (22.6%) were referring patients to non-accredited laboratories and remaining 17 (20.2%) were referring some patients to accredited and others to non-accredited ones. All but one family physician reported referring MDR-TB patients to specialists. The sole allopathic family physician who reported treating MDR-TB was following a standardised regimen followed by individualised after availability of drug sensitivity report. Four MD also were referring patients to CP and two MD did not provide details on management of MDR-TB.

Table 7 provides details of type of regimen prescribed for treating MDR TB by specialist. A total of 21 (50%) CP and 27 (60%) MD reported prescribing standardised regimen for all MDR-TB patients without testing for drug resistance to second line drugs. A total of 15 (35.7%) CP and 12 (26.7%) MD were using individualised regimen. Another 5 (11.9%) CP and 5 (11.1%) MD reported initiating patients on standardised or empiric regimen in the beginning and individualising later after availability of drug sensitivity reports.

270 **Table 7: Type of MDR-TB treatment regimens prescribed by specialists in private sector**
271

Regimen type	Chest physicians	Post-graduates in general medicine
	(n = 42)	(n = 45)
	No. (%)	No. (%)
Standardised	21 (50.0)	27 (60.0)
Empiric	1 (2.4)	1 (2.2)
Individualised	15 (35.7)	12 (26.7)
Standardised and then individualised	5 (11.9)	4 (8.9)
Empiric and then individualised	0 (0.0)	1 (2.2)

272

273 Detailed data on phases in treatment, duration of each phase and the combination of drugs used
274 for each phase were available for 24 CP and 34 MD. These regimens were compared with
275 standards laid down in ISTC and are presented in Table 8. Most practitioners (21, 87.5% CP and
276 25, 73.5% MD) reported using four drugs to which patient is known (results of susceptibility test) or
277 presumed to be susceptible (four new drugs). However, duration of use of injectable was four
278 months and total duration of treatment was 12 to 15 months in most cases. Only a quarter of the
279 specialists were prescribing injectable for six months and only about a third were prescribing
280 therapy for at least 18 months. Progress to treatment of MDR-TB was monitored by sputum culture
281 by 32 (76.2%) CP and 33 (68.8%) MD whereas another four (9.5%) CP and three (6.3%) MD
282 reported use of sputum smear microscopy. However, only six physicians mentioned need to
283 continue treatment for 12 to 18 months after culture conversion. Six (25.0%) CP and three (8.8%)
284 MD were prescribing ISTC recommended regimen.

285

286 **Table 8: Appropriateness of MDR-TB treatment regimens based upon International**
287 **Standards on Tuberculosis Care**
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Appropriateness of MDR-TB regimens	Chest physicians	Post-graduates in general medicine
	(n = 24)	(n = 34)
	No. (%)	No. (%)
Use of four drugs to which patient is known or presumed to be susceptible	21 (87.5)	25 (73.5)
Duration of treatment 18 months or more	10 (41.7)	11 (32.4)
Injectable drug for six months or more	7 (25.0)	8 (23.5)
Confirming with all three criteria*	6 (25.0)	3 (8.8)

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*As per ISTC standard 12

290 4. DISCUSSION

291

292 As stated earlier, studies over past two and half decade have documented variance in medical
293 practice and irrational use of anti-tubercular drugs in India and abroad. This study shows that the
294 use of irrational regimens continues in Mumbai's private sector and highlights variation in practice

among different physician groups. In contrast to most previous studies, many practitioners in this study reported using sputum smear microscopy for diagnosis; however, they did not necessarily rely on the results of same. Majority of CP and MD reported relying upon sputum smear microscopy for diagnosis of pulmonary TB whereas family physicians did not accord much importance to it. There is possibility of incorrectly interpreting respiratory symptoms and radiologic findings leading to unnecessary treatment with anti-tubercular drugs (27,28).

Family physicians were significantly less likely to use ISTC regimen. Family physicians are first point of care for most people and their current practices have public health implications. The sub-optimal regimens with rifampicin for less than six months and/ or absence of pyrazinamide were prescribed more often by FP. Such regimens are less likely to result in cure. On the other hand, regimens that include drugs other than those recommended by ISTC, although may be effective, has potential for two adversities. First, these additional drugs (often second-line) are associated with additional adverse effects. Secondly, in absence of mechanisms to ensure compliance patients often interrupt or discontinue treatment (9). This may result in bacilli developing resistance to second-line drugs which limits treatment options available, result in poor treatment outcomes and is associated with risk of transmission of DR-TB.

The study also noted that many practitioners were using drugs for longer duration than ISTC recommendation. These typically included use of ethambutol in continuation phase and total treatment duration of eight months. Standards for TB Care in India (STCI) now recommend use such regimens in India. Although, these regimens are not as per ISTC recommendation, they cannot be considered as inappropriate or irrational.

Given the high burden of drug-resistant cases in Mumbai, it is crucial to detect patients with drug resistance early both for treating them successfully as well as preventing transmission of drug-resistant forms. The study highlights delay in suspecting drug resistance in case of non-response to treatment. This study found that practices like initiating another regimen or extending same regimen for non-responders without investigating them for presence of drug resistance were common. Most common another regimen was addition of single drug streptomycin to failing first regimen; a practice in line with older RNTCP guidelines (25). However, in a city with high DR-TB burden, addition of single drug without testing for presence of drug resistance is not appropriate and is against one of the basic tenets of TB therapy (29). This is because such a regimen may not be able to treat MDR-TB if it exists. STCI (standard 7) cautions against use of single drug without drug sensitivity testing due to overwhelming evidence against same (26). Moreover, none of these other regimens prescribed before testing for drug resistance was found to be adequate (as per ISTC guidelines) for treatment of MDR-TB. There is need to sensitise private practitioners regarding need of suspecting and testing for drug resistance early and avoiding retreatment regimens without testing for presence of drug resistance.

Although, conventional solid culture and drug sensitivity testing is gold standard for diagnosis of drug resistance, the result is available with time lag of up to three months. Liquid cultures are not quick either requiring at least two months. Molecular diagnostic tests can address the problem of delay when offered as a point-of-care test in programme settings but detects resistance only against rifampicin and/ or isoniazide (30,31,32,33). Thus, although it tells regarding presence of MDR-TB, it does not differentiate between MDR-TB with XDR or other forms of DR-TB.

Many specialists in private sector in this study reported use of standardised regimens without testing for drug resistance for second line drugs. Such practice may not only be inadequate but also potentially accentuate drug resistance. Standardised regimens may be recommended only if prevalence of resistance to fluoroquinolone and injectable is low. Data on drug-resistance to drugs other than fluoroquinolone is limited and studies are needed in this direction. With respect to fluoroquinolones, a recent study from Mumbai showed that resistance to be 30% among cultures tested (34) providing evidence regarding presence of pre-XDR. Therefore, regimens should be individualised based on culture and sensitivity reports. Early diagnosis of DR-TB using molecular diagnostic tests supplemented by culture and sensitivity tests will help in individualising regimen. Such individualised regimen needs to be prescribed for adequate duration guided by culture reports.

What are possible solutions? Under, RNTCP the role of private providers was limited to suspecting and referral of patients so that all diagnosed cases could be provided DOTS under the

programme, monitored and followed up. However, in view of the evidence that patients do not wish to be receiving the government programme even in private sector, this strategy alone will be inadequate (7,20). There is need to train physicians with respect to correct treatment practices for new TB cases, suspect drug-resistance in time and in use of appropriate diagnostic and treatment regimens for drug-resistant TB. Needless to say, such trainings should be in line with evidence based standards for TB care.

Recently formulated Standards for TB Care in India (STCI) based upon scientific evidence in Indian epidemiological context provide an apt solution (26). In the city of Mumbai, renewal of registration for practicing medicine needs completion of hours of continued medical education (CME). STCI based training could be made mandatory part of same. Similar trainings could be mandated for practitioners from other streams as well.

There is also need to monitor TB management practices. Physicians should be mandated to maintain relevant data on diagnosis and treatment of TB patients. Currently, the private practitioners are mandated to notify every case of TB they are treating. The notification could include details of prescription and mobile technology may be used to record and transmit same. This may facilitate monitoring as well as identify practitioners in need of training. However, ethical aspects of such an intervention need to be debated as it may involve intrusion of privacy and breach of confidentiality (35).

Although not a part of this study, compliance to treatment for patients taking treatment in private sector is an important issue that merits attention. Patients who are informed about disease and treatment, patient centeredness of interactions with providers, social networks such as self-help groups or patient support groups, and appropriate technology such as mobile technology to monitor adherence may help in ensuring adherence to treatment (36,37).

The study had certain limitations. Many physicians refused to participate and this participation bias might have affected study findings. In our opinion, physicians not adhering to any guidelines are less likely to participate in such studies. There are thousands of family physicians practicing in the city but from feasibility point of view only those from three locations in city were selected which limits generalisability of results for family physicians. Some questions were not answered completely or left blank by study respondents and such responses had to be excluded from analysis for example timing of suspecting DR-TB after initiating treatment was not reported by many, mostly family physicians. Data on drug dosages was not collected and the findings are presented with an assumption that the drug dosages were correct. These limitations do not however override the fact that current management practices were not only inappropriate but also that their continuation may worsen drug resistance patterns.

5. CONCLUSION

The study shows that practices in private sector in Mumbai regarding management of TB deviate from international standards of care and are key drivers of DR-TB epidemic. Private sector needs to respond the changing epidemiological pattern of drug resistance and minimise delay in investigations for drug resistance. Failure to suspect drug resistance and diagnose DR-TB early is crucial factor that needs immediate attention. Rational use of anti-tubercular drugs for management of both drug-sensitive and resistant TB is essential for controlling the epidemic. Failure to learn from past mistakes will only replace MDR-TB with higher orders of drug resistance.

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