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Surveillance of drug-resistant tuberculosis in the state of Gujarat, India

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SUMMARY

BACKGROUND: Limited information about the prevalence of drug-resistant tuberculosis (TB) has been reported from India, the country with the world's highest burden of TB. We conducted a representative state-wide survey in the state of Gujarat (2005 population: 56 million).

METHODS: *Mycobacterium tuberculosis* isolates from a representative sample of new and previously treated smear-positive pulmonary TB (PTB) cases were subjected to drug susceptibility testing (DST) against first-line drugs at a World Health Organization supranational reference laboratory. Isolates found to have at least both isoniazid (INH) and rifampicin (RMP) resistance (i.e., multidrug-resistant TB [MDR-TB]) were subjected to second-line DST.

RESULTS: Of 1571 isolates from new patients, 1236 (78.7%) were susceptible to all first-line drugs, 173 (11%) had any INH resistance and MDR-TB was found in 37 (2.4%, 95%CI 1.6–3.1). Of 1047 isolates from previously treated patients, 564 (54%) were susceptible to all first-line drugs, 387 (37%) had any INH resistance and MDR-TB was found in 182 (17.4%, 95%CI 15.0–19.7%). Among 216 MDR-TB isolates, 52 (24%) were ofloxacin (OFX) resistant; seven cases of extensively drug-resistant TB (XDR-TB) were found, all of whom were previously treated cases.

CONCLUSION: MDR-TB prevalence remains low among new TB patients in Gujarat, but is more common among previously treated patients. Among MDR-TB isolates, the alarmingly high prevalence of OFX resistance may threaten the success of the expanding efforts to treat and control MDR-TB.

KEY WORDS: tuberculosis; drug resistance; India

THE FOURTH GLOBAL REPORT on Anti-tuberculosis Drug Resistance Surveillance found that the proportion of reported tuberculosis (TB) cases that exhibited any antibiotic resistance 'ranged from 0% in two Western European countries to 56.3% in Baku, Azerbaijan'.[1] The overall proportion of multidrug-resistant tuberculosis (MDR-TB), defined as TB resistant to at least isoniazid (INH) and rifampicin (RMP), with or without resistance to other first-line drugs, was 5.3%, ranging from 0% to 35% of reported TB cases. Based on the survey data, the World Health Organization (WHO) estimates that, globally, nearly half a million new cases of MDR-TB occur each year.[2] The report also found that extensively drug-resistant TB (XDR-TB), i.e., MDR-TB with resistance to a fluoroquinolone (FQ) and one of the injectable second-line drugs, which is more expensive and difficult to treat than MDR-TB, is widespread, with 45 countries having reported at least one case.[1] However, the WHO report cautions that few countries are currently equipped to diagnose XDR-TB, and it is therefore difficult to estimate the true extent of XDR-TB.[2]

India has the world's highest burden of TB (approximately 3.4 million cases), accounting for one fifth of global incident cases, and ranks first among the 22 TB high-burden countries.[3] Drug-resistant TB (DR-TB) has frequently been encountered in India, and its presence has been known since anti-tuberculosis drugs were first introduced for the treatment of TB. Most previous reports on drug resistance from India are from tertiary level care, and are thus not representative of the TB situation in India.[4] These reports are therefore of little use for the planning purposes of the Government of India's Revised National Tuberculosis Control Programme (RNTCP).

To guide the RNTCP, the first representative drug resistance survey was undertaken in Gujarat in 2005–2006, and the results are reported here.

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METHODS

Setting

The state of Gujarat, in the northwest of India, has a population of almost 56 million (2005). Gujarat began implementing the RNTCP in a phased manner in 1998, achieving state-wide coverage in April 2004. In 2006, over 77 000 patients were registered under the RNTCP in Gujarat, with a case detection rate of 69% and a treatment success rate of 86% among new smear-positive pulmonary TB (PTB) cases.[5] The laboratory used for the survey was the Tuberculosis Research Centre (TRC), Chennai, a WHO-designated Supranational Mycobacteriology Reference Laboratory, South-East Asian Region, and the National Reference Laboratory for the RNTCP. The survey was conducted with ethical approval from the RNTCP.

Training was given to all staff on all aspects of the survey, including collection, biosafe packing and transport of specimens, patient information and treatment history (to prevent misclassifications). The minimum and maximum delays in receiving specimens ranged from 2 to 66 days, with 80–90% of specimens received within 7–10 days (recovery rates from specimens transported in cetylpyridinium chloride [CPC] are being reported separately). The history of treatment was carefully collected and verified independently during the survey period, as the programme also performs routine monitoring (internal evaluations) of district level programmes that specifically looks at this issue. Minimal misclassifications were found in Gujarat.

Definitions

Resistance definitions were used as per the WHO guidelines.[6]

Study design

This was a cross-sectional cluster survey to estimate the prevalence of drug resistance among *Mycobacterium tuberculosis* isolates recovered from new and previously treated smear-positive PTB cases diagnosed in RNTCP microscopy centres in Gujarat, India, from November 2005 to October 2006. The survey was conducted in accordance with international recommendations for drug resistance surveillance.[6]

The basic sampling unit for clusters was the RNTCP microscopy centre. A sample size of 1680 new and 992 previously treated cases was estimated based on an expected MDR-TB prevalence of respectively 2% and 12%, with 50% precision, 10% loss and design effect of 2. Of 630 RNTCP microscopy centres, 52 (27 rural and 25 urban) were randomly selected after weighting by number of new cases; selected centres were assigned a fixed sample size per microscopy centre of 32 consecutive new smear-positive cases. Specimens obtained from patients suspected of TB were evaluated by Ziehl-Neelsen (ZN) at the microscopy centres; two additional specimens were collected from those patients with positive sputum smear results for culture and drug susceptibility testing (DST). Human immunodeficiency virus (HIV) testing was not done as part of the survey, as it was not policy at the time.

Treating physicians used a standardised reporting form to interview the smear-positive patients and abstracted medical records for information on history of previous anti-tuberculosis drug use. At each microscopy centre, enrolment continued of all consecutive smear-positive patients (new and previously treated) until a sample size of 32 new patients was reached. Forms were sent to the TRC, double-entered and analysed using Epi Info 6.04d (Centers for Disease Prevention and Control, Atlanta, GA, USA).

Culture and DST procedures

Sputum specimens, collected from eligible smear-positive patients at the microscopy centres in McCartney bottles with 1% CPC/2% sodium chloride, were transported to the reference laboratory. Concentrated deposit smears were prepared and stained with auramine phenol. Culture and DST were performed using solid Löwenstein-Jensen (LJ) media as per the National Drug Resistance Surveillance Survey Protocol.[7] For DST, pure drug powders are procured from Sigma Aldrich India Ltd., Bangalore, and the economic variant of the indirect proportion method was used, with critical concentrations of INH 0.2 μg/ml, streptomycin (SM) 4 μg/ml, RMP 40 μg/ml and ethambutol (EMB) 2 μg/ml. For internal quality control (IQC), each batch of DST for all drugs tested was accompanied by an H37Rv strain which was tested with the lower concentrations, along with one strain with known resistance to each drug.[8] In addition, DST was performed using two methods (proportion sensitivity and absolute concentration methods) for the initial 1200 samples of the survey; there was 98% concordance between the results.

For those isolates that were identified as MDR-TB, second-line DST for kanamycin (KM), ofloxacin (OFX) and ethionamide (ETH) was conducted on solid LJ media using the 1% proportion sensitivity method as per WHO guidelines,[9] using minimum critical concentrations of respectively 30 μg/ml, 2.0 μg/ml and 40 μg/ml. The IQC procedures followed were as for first-line DST. Proficiency testing for second-line drugs with the Supranational Reference Laboratory in Antwerp, Belgium, was available post-survey and had an agreement of >90%.

RESULTS

A total of 2674 patients (1979 males and 695 females) were enrolled and had specimens collected and sent to the TRC, including 1638 (61%) from new patients and 1126 (39%) from previously treated

Table 1 Prevalence of first-line anti-tuberculosis drug resistance among *M. tuberculosis* isolates from new and previously treated patients, Gujarat, India, November 2005–October 2006

	New cases		Previously treated	
	n (%)	95%CI	*n* (%)	95%CI
Total patients with DST results	1571 (100)		1047 (100)	
Susceptible to all four drugs (H+R+E+S)	1236 (78.7)		564 (53.9)	
Any resistance	335 (21)	19.3–23.4	485 (46.3)	43.1–49.2
H	173 (11)	9.4–12.6	387 (37.0)	34.0–39.9
R	40 (2.5)	1.8–3.3	192 (18.0)	16.0–20.0
E	30 (1.9)	1.2–2.6	107 (10.2)	8.4–12.0
S	228 (15)	12.8–16.3	276 (26.4)	23.7–29.0
Monoresistance	246 (15.7)	13.9–17.5	220 (21)	18.5–23.5
H only	84 (5.4)	4.2–6.5	122 (11.7)	9.7–13.6
R only	3 (0.2)	0.03–0.4	10 (1.0)	0.4–1.5
E only	3 (0.2)	0.03–0.4	0	0
S only	156 (10.0)	8.5–11.4	88 (8.4)	6.7–10.0
MDR-TB	37 (2.4)	1.6–3.1	182 (17.4)	15.0–19.7
Resistant to all 4 drugs (H+R+E+S)	13 (0.8)	0.4–1.3	69 (6.6)	5.1–10.0
Other patterns	52 (3)	2.4–4.2	83 (8)	6.3–9.6
H+E	3 (0.2)	0.03–0.4	7 (0.7)	0.18–1.2
H+S	45 (2.9)	2.0–3.7	66 (6)	4.8–7.8
H+E+S	4 (0.3)	0–0.5	10 (1)	0.4–1.6

CI = confidence interval; DST = drug susceptibility testing; H = isoniazid; R = rifampicin; E = ethambutol; S = streptomycin; MDR-TB = multidrug-resistant tuberculosis (defined as resistance to at least H and R).

patients. Overall smear positivity was 98.5%: 97% were smear- and culture-positive, 0.9% smear-negative and culture-positive, 1.8% were smear-positive and culture-negative and 0.7% were smear- and culture-negative. *M. tuberculosis* was recovered from respectively 1582 (97%) and 1067 (95%) new and previously treated cases. Of these, DST results were available from 1571 (99.3%) new and 1047 (98.1%) previously treated cases (Table 1). There were no significant differences in drug resistance patterns and age-sex distribution (data not shown). Smear positivity concordance between the ZN and fluorescent microscopy smears at the RNTCP microscopy centres and the TRC was 98.5%.

Resistance to first-line anti-tuberculosis drugs

Among new patients, 79% of all isolates were fully susceptible and 21% showed any resistance. Any INH resistance was 11% (95% confidence interval [CI] 9.4–12.5), and the prevalence of MDR-TB was 2.4% (95%CI 1.6–3.1). Resistance to INH, EMB and/or SM was 3% (95%CI 2.4–4.2); RMP resistance other than MDR-TB was rare, with just 0.2% monoresistance (Table 1).

Among previously treated patients, 54% of all isolates were fully susceptible and 46% showed any resistance. The prevalence of drug resistance was markedly higher than in the new patients. Any INH resistance was found in 37% (95%CI 34.0–39.8) and the prevalence of MDR-TB was 17.4% (95%CI 15.0–19.7). Similarly, compared to new patients, four-drug resistance (6.6%) was more common in previously treated patients (Table 1).

Second-line drug resistance among MDR-TB cases

A total of 219 MDR-TB cases were detected in the survey, of which respectively 37 and 182 were new and previously treated cases. The 216 second-line drug patterns available are shown in Table 2. Any resistance to OFX was found in 52 (24%, 95%CI 18.1–29.4) isolates. There was no significant difference in any OFX resistance between isolates from new or

Table 2 Prevalence of second-line drug resistance amongst multidrug-resistant *M. tuberculosis* isolates, Gujarat, India, November 2005–October 2006

Second-line DST	New cases (*n* = 37) *n* (%)	Previously treated cases (*n* = 179) *n* (%)	Total (*N* = 216) *n* (%)
Susceptible to all second-line drugs tested (OFX, KM, ETH)	18 (48.6)	101 (56.4)	119 (55.0)
Any resistance	19 (51.4)	75 (42.0)	94 (43.5)
KM	0	7 (4.0)	7 (3.2)
OFX	7 (19.0)	45 (25.0)	52 (24.0)
ETH	15 (40.5)	45 (25.0)	60 (28.0)
Monoresistance	16 (43.2)	56 (31.0)	72 (33.0)
KM only	0	0	0
OFX only	4 (11.0)	30 (17.0)	34 (16.0)
ETH only	12 (32.4)	26 (14.5)	38 (17.5)
XDR-TB	0	7 (4.0)	7 (3.0)
KM+OFX	0	4 (2.2)	4 (1.8)
KM+OFX+ETH	0	3 (1.7)	3 (1.4)
Other patterns	3 (8.0)	12 (7.0)	15 (7.0)
OFX+ETH	3 (8.0)	12 (7.0)	15 (7.0)

DST = drug susceptibility testing; OFX = ofloxacin; KM = kanamycin; ETH = ethionamide; XDR-TB = extensively drug-resistant TB (defined as an MDR-TB isolate also resistant to OFX and a second-line injectable class drug [e.g., KM]); MDR-TB = multidrug-resistant tuberculosis.

previously treated MDR-TB cases. Any resistance to ETH was found in 60 (27.8%, 95%CI 21.5–33.3) isolates, and was slightly more common among new MDR-TB cases compared to previously treated MDR-TB cases (relative risk [RR] 1.6, 95%CI 1.0–2.6). KM resistance was very uncommon, being found in only seven isolates (3.2%, 95%CI 0.9–5.5), all of which also had OFX resistance, and were thus classified as XDR-TB (3% of the total MDR-TB isolates). All instances of KM resistance and XDR-TB occurred in previously treated cases.

DISCUSSION

This is the largest population-based survey of the prevalence of drug-resistant TB to date from India, representative of TB patients treated under the RNTCP in Gujarat. We detected a low prevalence of MDR-TB among new patients (2.4%), similar to that previously reported, and much lower than reported from other high TB burden countries from the former Soviet Union[2] and China.[10] The prevalence of any resistance to INH (11%), SM (15.0%), RMP (2.5%) and EMB (2.0%) and MDR-TB observed among new cases are similar to levels seen in other previous district-level reports.[4,11–13] Levels of mono- and polyresistance are also lower than in most previous reports from India.[14,15] The findings from this survey and the consistency with previously reported results support the interpretation that standard short-course chemotherapy is likely to remain highly effective among the great majority of new TB patients in India.

For the first time, this survey provides a precise indication of the prevalence of drug resistance from a representative sample of previously treated patients in India. We found that 17.4% of previously treated patients had MDR-TB, and 6.6% had four-drug resistance. In 2006, more than 190 000 patients were registered as smear-positive PTB retreatment cases in India.[5] The WHO has estimated that over 110 000 MDR-TB cases emerged in India in 2006.[1] The RNTCP has acknowledged that, although MDR-TB cases represent a smaller proportion of the overall TB caseload in India, they constitute an ongoing problem for the programme from both an epidemiological and a human rights viewpoint.[16] The RNTCP has therefore developed a response plan that aims to continue strengthening the programme's preventive activities against the development of 'new' MDR-TB cases by providing high-quality DOTS services and introducing RNTCP DOTS-Plus Category IV services for MDR-TB cases in a phased manner across the country. The first MDR-TB patients were registered for RNTCP Category IV treatment in August 2007 in Gujarat itself.[17] Reaching all the smear-positive retreatment patients with culture and DST services, and treatment for those identified with MDR-TB, will be crucial to accelerate and sustain effective TB control efforts in India.

The strengths of this survey are its scale and representativeness and the inclusion of large numbers of previously treated patients. Most previous reports on anti-tuberculosis drug resistance from India have been from hospitals or tertiary care centres, and hence have not been representative of the wider community of TB patients. A small number of district-wide representative surveys carried out by the TRC and the National Tuberculosis Institute (NTI), Bangalore, between 1998 and 2002, covered much smaller geographical areas. The results reported here are quite consistent with those previously reported from the state of Gujarat[18,19] and other geographical areas throughout India.[4]

What are the risks of MDR-TB increasing in India? During the survey period, the RNTCP in Gujarat consistently achieved a new smear-positive case detection rate of over 70%, with a success rate of over 85%. Of the 2006 patient cohort, only 2.6% of new smear-positive cases failed treatment, suggesting that the thrice-weekly intermittent standard short-course chemotherapy regimen remains effective in India.[5] The elevated proportion of MDR-TB among previously treated cases also includes some chronic cases but, more importantly, a large proportion of retreatment patients were previously treated outside the RNTCP (80% of the patients are from the private sector and the non-RNTCP public sector), many of whom have received suboptimal TB treatment.[20] Treatment outcomes for previously treated cases in Gujarat are not satisfactory. While low treatment success among these patients is primarily due to high levels of default (20–24% in 2005–2006), it is also likely that high levels of any drug resistance (46%) and resistance to INH (37%) and SM (26%) played an important role.[17] Expanding access to culture and DST services for all smear-positive previously treated patients could be an efficient strategy to detect MDR-TB, initiate early treatment and prevent further transmission, as is being planned by the RNTCP.

Among MDR-TB isolates, we detected an alarming and unprecedented prevalence of any resistance to OFX of 24% (95%CI 18.4–29.7), which was not significantly different among new and previously treated MDR-TB patients (19% vs. 25%, Fisher's two-tailed test, $P = 0.56$). The high level of resistance to an FQ (i.e., OFX in this instance) correlates well with the very widespread use of FQs for the treatment of new TB cases in the private sector and its irrational use for pyrexia of unknown origin (PUO) and respiratory infections that could be undiagnosed TB in India. This is in line with other reports from elsewhere in the world where high rates of resistance to FQs are reported.[21–23] Case reports have shown that even a short duration of monotherapy with a FQ can quickly result in acquired resistance in *M. tuberculosis*.[24,25] Regardless of the reason, resistance to FQs has serious implications. First, FQs are crucial for the treatment of MDR-TB, and resistance to FQs has been

independently associated with poor MDR-TB treatment outcomes.[26] Patients with FQ resistance are also at risk of developing XDR-TB during treatment with second-line drugs, a risk that may increase if these drugs are administered outside the setting of a structured and supportive treatment programme.[27] Second, Phase III clinical trials are currently evaluating the effectiveness of FQs as first-line anti-tuberculosis drugs in shorter duration regimens.[28] If the prevalence of resistance to FQs increases substantially, the value of these drugs as an alternative first-line regimen could potentially be substantially reduced.

Although we could only test the MDR isolates against KM, resistance to KM was not observed in any of the MDR-TB isolates from new cases and was detected in only seven (4.0%, 95%CI 1.1–6.7) of the previously retreated cases. The level of KM resistance in previously treated patients is lower than reported elsewhere.[29] The low levels of KM resistance seen in Gujarat could be due to the very limited use of this drug in the private sector, and also because of the ease of prescribing an FQ.

Ethionamide (ETH) resistance was also high (28.0% overall, respectively 40.5% and 25% among new and treated cases). Resistance to ETH is difficult to interpret because technical issues with the DST make the results of limited reliability. Hence not all observed ETH resistance can be attributed to use of this drug in clinical settings,[30,31] as reported by others,[21] and the role of cross-resistance with INH due to mutations in the *inh*A gene and others.[32,33] A subset of such ETH-resistant isolates tested for the *inh*A gene showed a 40% prevalence of this mutation, which may account for the high in vitro resistance to ETH that was observed (unpublished data).

This survey had several limitations. For logistical reasons, isolates were collected only from patients who were smear-positive at an RNTCP microscopy centre, most of which are located in the public health system. Patients diagnosed outside the RNTCP, many of whom would not even have undergone smear microscopy, are not included here at the time of diagnosis. However, we also included retreatment patients, many of whom had no prior experience with TB treatment under the RNTCP. In the MDR isolates, only three of the major second-line drugs (ETH, KM and OFX) were tested, but the definition of XDR-TB also includes amikacin (AMK) and capreomycin (CPM) resistance. Our XDR-TB prevalence estimate, however, is likely to be accurate, as AMK resistance is highly concordant with KM and separate testing is usually not necessary,[34] while CPM was not available in India until very recently. Diagnostic centres for enrolment were selected weighted on the number of new patients, and only those retreatment patients attending the same diagnostic centres were enrolled consecutively. However, given the large number of previously treated patients enrolled and the random selection of microscopy centres, this is not likely to have affected the representativeness of the drug resistance prevalence estimates for previously treated patients.

CONCLUSION

This survey provides the first representative data to be reported on drug resistance prevalence at the community level in India, and of second-line drug resistance patterns amongst the MDR-TB cases identified in the survey. The results give an authentic picture of the levels of MDR-TB and XDR-TB in the setting of the RNTCP in India, and highlights the potential threat that the level of 'pre-XDR-TB' presents to the RNTCP Category IV regimen, due most likely to the widespread misuse of OFX outside the RNTCP for the treatment of both TB and non-TB patients in the country. India's RNTCP has taken cognisance of the high levels of MDR-TB and non-MDR drug resistance among retreatment cases and has developed a response plan that aims to continue strengthening the programme's preventive activities against the development of 'new' MDR-TB cases by provision of high-quality DOTS services throughout the country, improving public-private partnerships for TB treatment, quality assured laboratory services and the introduction of Category IV services for MDR-TB cases in the country.

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RÉSUMÉ

CONTEXTE : On ne dispose que d'informations limitées au sujet de la prévalence de la tuberculose (TB) à germes résistants en provenance de l'Inde, le pays du monde où le fardeau de la TB est le plus élevé. Nous avons mené une enquête représentative au niveau de l'Etat dans l'Etat de Gujarat (population en 2005 : 56 millions).

MÉTHODES : Les isolats de *Mycobacterium tuberculosis* provenant d'un échantillon représentatif des cas de TB pulmonaire (TBP) à bacilloscopie positive, nouveaux ou traités antérieurement, ont subi un test de sensibilité aux médicaments (DST) à l'égard des médicaments de première ligne dans un laboratoire de référence supranational de l'Organisation mondiale de la Santé. Les isolats où une multirésistance (TB-MDR, c'est-à-dire une résistance au moins à l'égard de l'isoniazide [INH] et de la rifampicine [RMP]) a été trouvée ont été soumis à un DST pour les médicaments de seconde ligne.

RÉSULTATS : Sur 1571 isolats provenant de nouveaux

cas, 1236 (78,7%) étaient sensibles à l'ensemble des médicaments de première ligne ; on a décelé n'importe quel type de résistance à l'INH dans 173 cas (11%) et on a trouvé une TB-MDR dans 37 cas (2,4% ; IC95% 1,6–3,1). Sur les 1047 isolats provenant de patients traités antérieurement, la sensibilité à l'ensemble des médicaments de première ligne a été observée dans 564 isolats (54%), une résistance quelconque à l'INH dans 387 isolats (37%) et une TB-MDR dans 182 isolats (17,4% ; IC95% 15,0–19,7). Parmi les 216 isolats TB-MDR, on a observé une résistance à l'ofloxacine (OFX) dans 52 cas (24%) et une TB avec germes ultrarésistants (TB-XDR) dans sept cas, dont tous étaient des cas traités antérieurement.

CONCLUSION : A Gujarat, dans les nouveaux cas de TB, la prévalence de la TB-MDR reste faible, mais elle est plus courante chez les patients traités antérieurement. Parmi les isolats de TB-MDR, la prévalence élevée et alarmante de la résistance à l'OFX peut mettre en péril le succès de l'extension des efforts pour traiter et contrôler la TB-MDR.

RESUMEN

MARCO DE REFERENCIA : Existen pocos informes sobre la prevalencia de tuberculosis (TB) farmacorresistente en India, el país con la más alta carga de morbilidad por esta enfermedad. Se llevó a cabo un estudio representativo de alcance estatal en Gujarat (población de 56 millones en 2005).

MÉTODOS : En un laboratorio supranacional de referencia de la Organización Mundial de la Salud, se practicaron pruebas de sensibilidad a los medicamentos antituberculosos de primera línea en una muestra representativa de aislados de *Mycobacterium tuberculosis* provenientes de casos nuevos y casos previamente tratados de tuberculosis pulmonar (TBP) con baciloscopia positiva. En los aislados que exhibieron resistencia como mínimo a isoniazida (INH) y a rifampicina (RMP) (TB-MDR), se realizaron además pruebas de sensibilidad a los antituberculosos de segunda línea.

RESULTADOS : De los 1571 aislados de pacientes nuevos, 1236 (78,7%) fueron sensibles a todos los antituberculosos de primera línea, 173 (11%) presentaron resistencia a INH y se encontró MDR en 37 (2,4% ; IC95% 1,6–3,1%). De los 1047 aislados provenientes de pacientes previamente tratados, 564 (54%) fueron sensibles a todos los medicamentos de primera línea, 387 (37%) resistentes a INH y 182 exhibieron MDR (17,4% ; IC95% 15,0–19,7). De los 216 aislados de TB-MDR, 52 (24%) presentaron resistencia a ofloxacina (OFX) ; se encontraron siete casos de TB extensivamente drogorresistente, todos en pacientes con antecedente de tratamiento antituberculoso.

CONCLUSIÓN : La prevalencia de TB-MDR sigue siendo baja en los pacientes diagnosticados como casos nuevos de TB en el estado de Gujarat, pero es más frecuente en los pacientes previamente tratados. La prevalencia inquietantemente alta de resistencia a OFX en los aislados de TB-MDR puede poner en peligro el éxito de las iniciativas de ampliación del tratamiento y el control de este tipo de TB.