Non-response to first-line anti-tuberculosis treatment in Sikkim, India: a risk-factor analysis study

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<http://dx.doi.org/10.5588/pha.18.0026>

Setting: Sikkim, India, has the highest proportion of tuberculosis (TB) patients on first-line anti-tuberculosis regimens with the outcome 'failure' or 'shifted to regimen for multidrug-resistant TB (MDR-TB)'.

Objective: To assess the factors associated with non-response to treatment, i.e., 'failure' or 'shifted to MDR-TB regimen'.

Methods: We conducted a retrospective cohort study using Revised National Tuberculosis Control Programme data of all TB patients registered in 2015 for first-line TB treatment. In addition, we interviewed 42 patients who had not responded to treatment to ascertain their current status.

Results: Of 1508 patients enrolled for treatment, about 9% were classified as non-response to treatment. Patient factors associated with non-response were urban setting (adjusted odds ratio [aOR] 2.39, 95%CI 1.22–4.67), ethnicity (being an Indian tribal, aOR 1.73, 95%CI 1.17–2.57, Indian [other] aOR 1.83, 95%CI 1.29–2.60 compared to patients of Nepali origin) and those on retreatment (aOR 2.40, 95%CI 1.99–2.91). Of the patients interviewed, 28 (67%) had received treatment for drug-resistant TB.

Conclusion: In Sikkim, one in 11 patients had not responded to first-line anti-tuberculosis treatment. Host-pathogen genetics and socio-behavioural studies may be required to understand the reasons for the differences in non-response, particularly among ethnic groups.

Tuberculosis (TB) remains a major public health problem worldwide. As of 2016, the global incidence of TB was estimated to be 10.4 million cases.¹ India tops the list of the 22 high TB burden countries, with 2.8 million cases (27% of the global burden) and about half a million deaths annually.^{1,2} The response to anti-tuberculosis treatment is crucial, as it not only determines the survival of the patient, it also reflects the effectiveness of the health system.³ Poor response of TB patients to first-line TB treatment indicates drug resistance, inappropriate treatment or poor treatment adherence, and it can affect TB elimination goals. In addition, it is well known that treatment outcomes are affected by factors such as age, sex, human immunodeficiency virus (HIV) status, diabetes, nutritional status and smoking.^{4–14}

India implemented the Revised National Tuberculosis Control Programme (RNTCP) in 1997. Sputum smear microscopy is the primary tool for TB diagnosis. In case of presumptive drug-resistant TB, sputum sam-

ples are simultaneously sent for culture and drug susceptibility testing (CDST). As it takes several days for the test results to become available, patients are initiated on first-line treatment. If resistance is diagnosed, treatment is initiated for multidrug-resistant TB (MDR-TB).

Treatment outcomes are based upon the patients' response to first-line anti-tuberculosis treatment (Table 1). At months 2 or 5 of treatment, a positive sputum smear test signifies that the patient is not responding to first-line treatment and tests for drug resistance are initiated. If the results confirm resistance to isoniazid and/or rifampicin, the patient is moved to MDR-TB treatment. Treatment outcomes of TB patients are reported 1 year after treatment initiation.

According to the RNCTP's annual TB report, nearly 1% of new smear-positive patients and 5% of smear-positive retreatment patients were 'moved to MDR-TB treatment' in 2016. The state of Sikkim drew the attention of the TB fraternity, as respectively 16% and 23% of new and retreatment smear-positive patients moved to MDR-TB treatment (the total number of TB patients in the state was approximately 1500), which was unusually high compared to the national average. These figures are extraordinary even compared to high MDR-TB burden states such as Maharashtra, where the rates were respectively 2% and 9%,² thus leading to speculation in terms of the quality of programme implementation, the quality of drugs supplied to the region and the type of *Mycobacterium tuberculosis* strains circulating in the area. The foremost aim was to investigate factors associated with non-responsiveness to treatment in TB patients and their status after 1 year of treatment.

We therefore conducted this study to determine 1) the sociodemographic and clinical factors associated with non-response to first-line treatment, and 2) the status of patients who had not responded to first-line treatment 1 year after their treatment outcome was notified, to investigate whether they were evaluated for drug resistance and if they were responding to MDR-TB treatment.

METHODOLOGY

Study design

This was a retrospective cohort study using routine programme data and a sample patient survey (interviews) based on a semi-structured questionnaire to ascertain their current treatment status.

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ACKNOWLEDGEMENTS

The article was developed as part of the National Operational Research Course (2016–2017) conducted by the International Union Against Tuberculosis and Lung Disease, Paris, France, in collaboration with National TB Institute, Bangalore; the Central TB Division, Ministry of Health and Family Welfare, Government of India, New Delhi, India; and the Centre for Disease Control, Atlanta, GA, USA. The course was conducted with the support of the Global Fund, Geneva, Switzerland. The authors thank the State TB Office of Sikkim for their support in conducting the study; and all District TB officers and RNTCP staff of the state of Sikkim who were part of our study group. Conflicts of interest: none declared.

KEY WORDS

MDR-TB; Indian tribal; Sikkim

Received 23 April 2018
Accepted 6 September 2018

PHA 2018; 8(4): 162–168
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TABLE 1 Definitions of treatment outcomes in accordance with RNTCP guidelines

Cured: initially sputum smear-positive patient who has completed treatment and has had two negative sputum smears, one of which was at the end of the treatment
Treatment completed: initially sputum smear-positive patient who has completed treatment with negative smears at the end of the intensive phase/2 months in the continuation phase, and no smears positive at the end of treatment
Or
Initially sputum smear-negative patient who has received a full course of treatment and has not become smear-positive at the end of treatment
Or
A patient with extra-pulmonary TB who has received a full course of treatment and has not become smear-positive during or at the end of treatment
Died: patient who died during the course of treatment regardless of cause
Failure: any TB patient who is smear-positive at ≥ 5 months after initiating treatment and not put on MDR-TB treatment
Lost to follow-up: a patient whose treatment has been interrupted for ≥ 2 consecutive months
Transferred out: a patient who has been transferred to another TB Unit and whose treatment outcome is not available
Moved to MDR-TB treatment: a patient who has been diagnosed as having MDR-TB by an RNTCP-accredited laboratory, before being declared a 'treatment failure', and is placed on the RNTCP MDR-TB treatment regimen

RNTCP = Revised National Tuberculosis Control Programme; TB = tuberculosis; MDR-TB = multidrug-resistant TB.

Study population

All TB patients enrolled with the Sikkim State TB programme in 2015 were included. Patient interviews were conducted for a random sample of patients identified as non-response to treatment.

Study period

The study was conducted from November 2016 to May 2017.

Study settings

The state of Sikkim is located in the hilly North-Eastern part of India, with a population of about 0.6 million spread over 7096 km². The state shares international borders with China, Nepal and Bhutan. Sikkim state is divided into four administrative districts, each with a district hospital and district TB centre (programme management unit for TB at district level). The health care services are predominantly delivered by the public health system, and there are 24 primary health centres and 147 subcentres (primary level health care), two community health centres and four district hospitals (secondary level health care) and one referral hospital.

The ethnicity of the Sikkim population is unique, with the majority being of Nepali ethnic origin. The indigenous tribes of Lepchas, Bhutias and Sherpas make up the remainder. A small proportion of the population is from other parts of India.¹⁵

Specific setting

The RNTCP was implemented in the state of Sikkim in 2002, and programmatic management of drug-resistant TB (PMDT) was initiated in 2012. Unlike the rest of India, Sikkim does not have a thriving private health sector, and the majority of the patients are therefore diagnosed and treated under the public health system only. The state has five RNTCP districts, 31 designated microscopy centres (DMCs), 598 DOT (directly observed treatment) cen-

TABLE 2 Case definitions in accordance with Revised National Tuberculosis Control Programme treatment guidelines

Case definitions

Pulmonary TB, smear-positive: pulmonary TB in a patient with at least one AFB smear-positive of the two initial sputum smear examinations using direct microscopy

Pulmonary TB, smear-negative: patient with symptoms suggestive of TB with two smear examinations negative for AFB, with evidence of pulmonary TB using microbiological methods (positive on culture or on other approved molecular methods) or smear-negative pulmonary TB on chest X-ray is classified as having

Extra-pulmonary TB: TB in any organ other than lungs (e.g., pleura, lymph nodes, intestine, genito-urinary tract, joint and bones, meninges of the brain, etc.)

Types of cases

New: a patient who has never undergone treatment for TB or has taken anti-tuberculosis drugs for <1 month

Relapse: a patient who was declared cured or treatment completed by a physician and who reports back to the health facility and is now found to be sputum smear-positive

Transferred in: a patient who has been received for treatment in a TB Unit after starting treatment in another unit where s/he has been registered

Treatment after default/loss to follow-up: a patient who has received treatment for TB for ≥ 1 month from any source and returns for treatment after having defaulted, i.e., not taken anti-tuberculosis drugs consecutively for $\geq 1-2$ months and found to be smear-positive

Treatment failure: any TB patient who is smear-positive at ≥ 5 months after initiation of treatment

TB = tuberculosis; AFB = acid-fast bacilli.

tres, one drug-resistant TB (DR-TB) centre, one intermediate referral laboratory and 16 cartridge-based nucleic-acid amplification test (CBNAAT) machines to detect DR-TB. However, as there are no culture or DST facilities in the state, samples are sent to national referral laboratories in New Delhi and Bangalore.

The operational definition for determining the type of TB cases and treatment outcomes are described in the Tables 1 and 2, respectively. In this study, we defined 'treatment non-response' as those new or retreatment patients who had undergone at least 30 days of first-line treatment and whose treatment outcomes were declared to be 'failure' or 'moved to MDR-TB treatment'.

Data collection, variables and analysis

Data were collected from TB treatment registers, DMC laboratory registers and referral for treatment registers. Randomly selected patients were interviewed using the semi-structured questionnaire by trained personnel. The key variables for each patient included age, sex, ethnicity, district, type of settlement, type of TB, date of diagnosis, date of treatment initiation, treatment regimen used, number of missed doses, treatment outcomes and date of treatment outcomes.

Data were double-entered and validated using EpiData entry software v 3.1 (EpiData Association, Odense, Denmark). After validation, the data were cleaned; missing data were labelled 'not recorded' for each variable. The data were then analysed using EpiData analysis software v 2.2.2.178. The data were summarised as numbers and percentages. Logistic regression was used to obtain odds ratios (ORs) and adjusted ORs using STATA v 12 (Stata Corporation, College Station, TX, USA) to identify factors associated with treatment non-response.

To ascertain current treatment status, all patients with treatment non-response were line-listed and 42 patients were ran-

domly selected for interview after providing informed consent. The principal investigator, who was the state programme manager for TB, and her team traced and contacted all 42 patients and interviewed them using a semi-structured questionnaire. Those patients who could not be met in person were contacted via mobile telephone. Patients' current treatment status is presented using a schematic representation (Figure 2).

Ethics

Ethics approval was obtained from Sir Thodup Namgyal Memorial Hospital, Gangtok, India, and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. Patients were interviewed after providing written informed consent, or verbal consent for those patients interviewed by telephone. No personal identifiers were used in the analysis.

RESULTS

Demographic and clinical profile of patients

In 2015, a total of 1508 TB patients were registered for treatment under the programme. Complete data were available for 1490 patients and included in the analysis. Patients' sociodemographic and clinical characteristics are shown in Table 3; 53% (793) were males and 63% (944) were from rural areas. About 80% ($n = 1190$) were new TB cases, 41% ($n = 618$) were smear-positive and 33% ($n = 499$) had extra-pulmonary TB; 7% ($n = 109$) were known diabetics and five were HIV-positive. The majority (75%) were of Nepali origin, and 18% were Indian tribal.

Treatment outcomes

Of the 1490 patients, complete treatment outcome data were available for 1464. Treatment outcomes, disaggregated by type of TB and case type, are presented in Table 4. Overall, 32% were cured, 52% completed treatment, 1% were lost to follow-up, 3% died, 9% switched to MDR-TB treatment and 2% failed treatment.

Patients who moved to MDR-TB treatment and those with outcome failure were considered patients with treatment non-response ($n = 159$). Among those who moved to MDR-TB treatment, 19 newly diagnosed patients (12%) received <30 days of first-line treatment. These were presumptive MDR-TB cases and were initiated on first-line anti-tuberculosis treatment while awaiting DST results. As the treatment duration of six patients could not be determined, these patients were excluded ($n = 25$), and a final 134 patients satisfied our criteria for 'non-response' to TB treatment (Figure 1).

Treatment initiation and adherence

Data on treatment initiation were available for 1405 patients. More than 80% were initiated on treatment within 1 week; the proportion was the same among the response and the non-response group. Information on treatment adherence in terms of any missed doses during the intensive phase of treatment was available for only 104 patients in the non-response group. Overall treatment adherence during the intensive phase was 98%. Most of the responders (99%) and only 74% of the non-responders had taken all the doses. As data in the non-response group were limited, we did not conduct further analyses.

Patients with non-response to first-line drugs and risk factors for non-response

Based on the study definition, patients were categorised into two groups: 1255 (cured, $n = 474$; treatment completed, $n = 781$) in the treatment response group and (failed, $n = 22$; 'moved to MDR-TB treatment', $n = 111$) 134 in the non-response group.

TABLE 3 Sociodemographic and clinical characteristics of TB patients registered in Sikkim state, 2015 ($n = 1490$)

Variable	<i>n</i> (%)
Sex	
Male	793 (53)
Female	697 (47)
Age group, years	
0–14	98 (7)
15–24	532 (36)
25–34	359 (24)
35–44	164 (11)
45–54	145 (10)
55–64	95 (6)
≥65	97 (7)
Place of residence	
Rural	944 (63)
Urban	546 (37)
Population group	
Nepali	1117 (75)
Indian tribal	273 (18)
Indian Other	100 (7)
Type of TB case	
New	1190 (80)
Relapse	133 (9)
Failure	17 (1)
Treatment after loss to follow-up	8 (1)
Other	132 (9)
Not recorded	10 (1)
Type of TB	
Pulmonary smear-positive	618 (41)
Pulmonary smear-negative	357 (24)
Extra-pulmonary	499 (33)
Not recorded	16 (1)
HIV status	
Positive	5 (0)
Negative	1339 (90)
Unknown	2 (0)
Not recorded	144 (10)
Diabetes status	
Positive	109 (7)
Negative	1188 (80)
Not recorded	193 (13)

TB = tuberculosis; HIV = human immunodeficiency virus.

The association between various sociodemographic variables and non-response are given in Table 5. Independently associated factors were being from an urban area (aOR 2.39, 95%CI 1.22–4.67; $P = 0.010$), ethnicity (being an Indian tribal, aOR 1.73, 95%CI 1.17–2.57; $P = 0.006$; Indian [other] aOR 1.83, 95%CI 1.29–2.60; $P = 0.001$) and retreatment cases (aOR 2.40, 95%CI 1.99–2.91; $P < 0.001$).

Status of patients with treatment non-response 1–2 years after treatment outcome notification

The status of 42 patients who were interviewed, disaggregated by their initial treatment outcome ('moved to MDR-TB treatment' or 'failed') is shown in Figure 2. Over 80% of the patients interviewed had pulmonary TB and were newly diagnosed. Overall, 28 (67%) patients were on MDR-TB treatment or had completed treatment. Of these, 20 were from the subgroup 'moved to MDR-TB treatment' and eight from the subgroup 'treatment failure'. It should

TABLE 4 Treatment outcomes of tuberculosis patients enrolled for treatment under the RNTCP in Sikkim state, disaggregated by type of TB, 2015 (*n* = 1464)*

	Overall (<i>n</i> = 1464) <i>n</i> (%)	New cases (<i>n</i> = 1179)		Retreatment cases (<i>n</i> = 156)		Other (<i>n</i> = 129)	
		Microbiologically confirmed (<i>n</i> = 461) <i>n</i> (%)	Clinically confirmed (<i>n</i> = 718) <i>n</i> (%)	Microbiologically confirmed (<i>n</i> = 150) <i>n</i> (%)	Clinically confirmed (<i>n</i> = 5) <i>n</i> (%)	Microbiologically confirmed (<i>n</i> = 2) <i>n</i> (%)	Clinically confirmed (<i>n</i> = 127) <i>n</i> (%)
Cured	472 (32)	355 (77)	13 (2)	102 (67)	0	0	2 (3)
Completed	764 (52)	2 (0)	654 (91)	2 (1)	4 (80)	0	102 (80)
Lost to follow-up	20 (1)	6 (1)	5 (1)	6 (4)	0	0	3 (2)
Failed	22 (2)	18 (4)	3 (0)	1 (0.7)	0	0	0
Moved to MDR-TB treatment	133 (9)	67 (15)	18 (3)	34 (22)	1 (20)	2 (0)	11 (9)
Died	42 (3)	9 (2)	19 (3)	6 (4)	0	0	8 (6)
Transferred out	11 (1)	4 (1)	6 (1)	0	0	0	1 (0.8)
Not recorded	1 (0)	0	0	1 (0)	0	0	0
Total	1464						

*Data for 26 patients were not available and were therefore not included in the table.

RNTCP = Revised National Tuberculosis Control Programme; TB = tuberculosis; MDR-TB = multidrug-resistant TB.

FIGURE 1 Flow chart showing identification of patients who failed to respond to first-line anti-tuberculosis treatment in Sikkim state, 2015. TB = tuberculosis.

be noted that 8/22 patients (36%) from the treatment failure group were moved to MDR-TB treatment after considerable first-line anti-tuberculosis treatment (>5 months).

DISCUSSION

This is one of the first studies conducted in the state of Sikkim to study risk factors for non-response to first-line treatment. Our study reports that 9% of patients had non-response to first-line treatment. The main strength of the study was the inclusion of all patients enrolled for treatment and use of routine programme records. The RNTCP supervision and monitoring systems, including periodic verification of the accuracy and consistency of the recording and reporting systems, are in place and functional in Sikkim. We therefore strongly believe that there are unlikely to be any major errors in the data, and that inferences made from these data reflect ground realities. The main limitation of the study is

that most of our study variables on patient factors were restricted to those that are routinely collected and documented in programme records. As several other patient factors or health system factors can affect study outcomes, such as socio-economic status, baseline drug resistance status, availability and functional status of culture and CDST services, etc., we are unable to account for these factors in our analysis and interpretation of the data. Another study limitation was the inability to reach all patients due to difficult terrain, communication issues and lack of adequate transport in the state.

Despite the above limitations, the study findings have the following implications on policies, practices and future research.

First, about 12% of new/retreatment patients who were moved to MDR-TB treatment within the first month were initiated on first-line treatment while waiting for their CDST results. As the state lacks CDST facilities, sending the samples to national laboratories delays the results. The RNTCP in Sikkim must ensure that access to CDST facilities is improved, either by identifying national centres that are closer to Sikkim State or by developing these facilities within the state so that patients are promptly initiated on correct anti-tuberculosis regimens. However, we appreciate the current practice of enrolling all patients who are initiated on first-line treatment in the TB register, which indicates good accountability. This documentation also diminishes the risk of pre-treatment loss to follow-up.¹⁶

Second, treatment non-response could be due to primary drug resistance or development of DR-TB during first-line treatment due to poor treatment adherence. Based on the limited adherence data that we collected (which showed good adherence), we are inclined to suggest primary drug resistance as the most likely reason for non-response. As the RNTCP currently advocates universal DST before the initiation of anti-tuberculosis treatment,¹⁶ the Sikkim RNTCP unit has begun to implement this policy in the state using Xpert® MTB/RIF (Cepheid, Sunnyvale, CA, USA) technology.

Third, factors associated with non-response included being from an urban area, retreatment TB and ethnicity. While the association between the first two factors is widely known,⁴⁻¹⁴ the association between ethnicity (Indian tribal vs. patients of Nepali origin) and non-response is new. Ethnicity is known to cause

TABLE 5 Risk factors for non-response to first-line treatment among TB patients registered in Sikkim state, 2015

Variable	Responders (<i>n</i> = 1255) <i>n</i> (%)	Patients with non-response (<i>n</i> = 134) <i>n</i> (%)	aOR (95%CI)	<i>P</i> value
Sex				
Female	580 (90)	64 (10)	Reference	
Male	675 (91)	70 (9)	0.93 (0.73–1.18)	0.562
Population group				
Nepali	957 (91)	89 (9)	Reference	
Indian tribal	221 (87)	32 (13)	1.73 (1.17–2.57)*	0.006*
Indian (other)	77 (86)	13 (14)	1.83 (1.29–2.60)*	0.001*
Place of residence				
Rural	819 (93)	66 (7)	Reference	
Urban	436 (87)	68 (13)	2.39 (1.22–4.67)*	0.010*
Case type				
New	1034 (93)	81 (7)	Reference	
Retreatment and others	221 (81)	53 (19)	2.40 (1.99–2.91)*	<0.001*
Type of TB				
Pulmonary smear-positive	463 (82)	103 (18)	Reference	
Pulmonary smear-negative	317 (95)	18 (5)	0.09 (0.04–0.22)*	<0.001*
Extra-pulmonary	463 (98)	10 (2)	0.25 (0.18–0.34)*	<0.001*
Diabetes				
No	1025 (91)	97 (9)	Reference	
Yes	86 (90)	10 (10)	0.89 (0.62–1.27)	0.530

*Statistically significant.

TB = tuberculosis; aOR = adjusted odds ratio; CI = confidence interval.

FIGURE 2 Flow diagram showing the status of a random sample of patients with non-response to first-line anti-tuberculosis treatment registered in 2015 and followed up after 2 years of treatment outcome declaration in Sikkim state. MDR-TB = multidrug-resistant tuberculosis; XDR-TB = extensively drug-resistant TB.

variations in susceptibility to tuberculous infection and progression to TB disease due to differences in sociobehavioural characteristics and/or genetic make-up.^{17–19} However, whether ethnicity can influence non-response to treatment and affect the pathway to non-response is unknown. Future research into this area is required to untangle the mystery of the very high non-response rate in Sikkim. Various host-pathogen genetic aspects are also

likely to cause drug resistance, disease susceptibility or progression to active disease.^{20–22} The Indian Council of Medical Research (New Delhi, India), the leading government research organisation, and the RNTCP are planning to undertake a genetic study to identify host-pathogen genetic factors associated with TB/MDR-TB in Sikkim.²³ While we welcome this approach, we believe that it is also essential to undertake anthropo-

logical studies to assess sociobehavioural differences among the various ethnic groups that could be associated with non-response to treatment.

Finally, the findings from interviews with patients with treatment non-response suggest that the majority were on or had completed treatment for DR-TB. This to a large extent allayed our fears about the status of these patients as to whether or not they had received or were receiving appropriate TB care.

CONCLUSION

In Sikkim, one in 11 patients had not responded to first-line anti-tuberculosis treatment. Ethnic origins (Indian tribal and Indian other) were associated with treatment non-response. Further genetic studies are needed to ascertain the relationship between ethnicity and non-response. CDST facilities should be established within the state for early diagnosis of drug-resistant TB.

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Contexte : L'état de Sikkim, en Inde, a la proportion la plus élevée du pays de patients atteints de tuberculose (TB) sous protocole antituberculeux de première ligne avec pour résultats « échec » ou « passé à un protocole de TB multirésistante (TB-MDR) ».

Objectif : Evaluer les facteurs associés à une non réponse au traitement (« échec » ou « passé à un protocole de TB-MDR »).

Méthode : Nous avons réalisé une étude rétrospective de cohorte grâce aux données du programme national révisé pour la lutte contre la tuberculose de tous les patients TB enregistrés en 2015 pour un traitement de TB de première ligne. Nous avons également interviewé 42 patients ayant une non réponse au traitement pour vérifier leur statut actuel.

Résultats : Sur les 1508 patients enrôlés en traitement, environ 9% ont été classés comme non réponse au traitement. Les facteurs liés au

patient associés à l'absence de réponse ont été un contexte urbain (odds ratio ajusté [ORa] 2,39 ; IC95% 1,22–4,67), l'ethnicité (appartenance à une tribu Indienne, ORa 1,73 ; IC95% 1,17–2,57, autres populations Indiennes, ORa 1,83 ; IC95% 1,29–2,60, par comparaison aux patients d'origine Népalaise) et aux patients en retraitement de TB (ORa 2,40 ; IC95% 1,99–2,91). Parmi les patients interrogés, 28 (67%) ont reçu un traitement pour TB pharmacorésistante.

Conclusion : Au Sikkim, un patient sur 11 avait une non réponse au traitement antituberculeux de première ligne. Des études de génétique hôte-pathogène et des études sociocomportementales pourraient être requises afin de comprendre les raisons des différences dans la non réponse, surtout entre les groupes ethniques.

Marco de Referencia: El estado de Sikkim en la India presenta la proporción más alta de pacientes cuyo desenlace del tratamiento antituberculoso de primera línea se clasifica como 'fracaso' o 'cambiado a un esquema contra la tuberculosis multirresistente (TB-MDR)'.

Objetivo: Evaluar los factores que se asocian con la falta de respuesta al tratamiento ('fracaso' o 'cambiado a un esquema contra la TB-MDR').

Métodos: Se llevó a cabo un estudio de cohortes, a partir de los datos del Programa Revisado Nacional contra la Tuberculosis, de todos los pacientes registrados en el 2015 en tratamiento antituberculoso de primera línea. Además, se entrevistaron 42 pacientes (que no respondieron al tratamiento), con el fin de verificar su situación actual.

Resultados: De los 1508 pacientes inscritos para tratamiento, cerca del 9% se clasificaron sin respuesta al tratamiento. Los factores del

paciente que se asociaron con la falta de respuesta fueron los siguientes: un entorno urbano (OR ajustado [ORa] 2,39; IC95% 1,22–4,67), la etnia (pertenencia a grupos tribales, ORa 1,73; IC95% 1,17–2,57 u otras poblaciones indias ORa 1,83; IC95% 1,29–2,60 cuando se compararon con los pacientes de origen nepalés) y el retratamiento antituberculoso (ORa 2,40; IC95% 1,99–2,91). De los pacientes entrevistados, 28 habían recibido tratamiento por TB farmacorresistente (67%).

Conclusión: En Sikkim, uno de cada 11 pacientes no respondió al tratamiento de primera línea contra la TB. Se precisarían estudios genéticos de la interacción entre el hospedero y el patógeno y estudios sociales conductuales que permitan comprender las razones de las diferencias en la falta de respuesta, sobre todo entre los diferentes grupos étnicos.