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Diverse clinical and social circumstances: developing patient-centred care for DR-TB patients in South Africa

L. Mitrani,[1] L. Dickson-Hall,[1] S. Le Roux,[1] J. Hill,[2] M. Loveday,[3,4] A. D. Grant,[2,5] K. Kielmann,[6] K. Mlisana,[7] M. Moshabela,[8] M.P. Nicol,[1,9,10] J. Black,[11,12] H. Cox[1,9]

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OBJECTIVE: To describe the medical, socio-economic and geographical profiles of patients with rifampicin-resistant TB (RR-TB) and the implications for the provision of patient-centred care.

SETTING: Thirteen districts across three South African provinces.

DESIGN: This descriptive study examined laboratory and healthcare facility records of 194 patients diagnosed with RR-TB in the third quarter of 2016.

RESULTS: The median age was 35 years; 120/194 (62%) of patients were male. Previous TB treatment was documented in 122/194 (63%) patients and 56/194 (29%) had a record of fluoroquinolone and/or second-line injectable resistance. Of 134 (69%) HIV-positive patients, viral loads were available for 68/134 (51%) (36/68 [53%] had viral loads of >1000 copies/ml) and CD4 counts were available for 92/134 (69%) (20/92 [22%] had CD4 <50 cells/mm^3). Patients presented with varying other comorbidities, including hypertension (13/194, 7%) and mental health conditions (11/194, 6%). Of 194 patients, 44 (23%) were reported to be employed. Other socio-economic challenges included substance abuse (17/194, 9%) and ill family members (17/194, 9%). Respectively 13% and 42% of patients were estimated to travel more than 20 km to reach their diagnosing and treatment-initiating healthcare facility.

CONCLUSIONS: RR-TB patients had diverse medical and social challenges highlighting the need for integrated, differentiated and patient-centred healthcare to better address specific needs and underlying vulnerabilities of individual patients.

South Africa is among the 20 countries with the highest estimated numbers of individuals with TB, TB-HIV comorbidity and multidrug-resistant or rifampicin-resistant TB (MDR-/RR-TB) worldwide. More than 13,000 individuals were diagnosed with MDR-/RR-TB and more than 9,000 treated in South Africa in 2018.[1] In 2011, in response to high local burden, South Africa introduced a national policy for the decentralisation of drug-resistant TB (DR-TB) treatment with the aim of reducing time to treatment and costs, and improving retention in care.[2] Decentralisation has been shown to be more cost-effective for health systems than centralised systems without compromising quality of care[3–5] and in reducing time to initiation, which can potentially reduce ongoing transmission risk.[6]

However, decentralisation does not address all barriers to treatment access and retention in care. Globally, there is a growing appeal to deliver patient-centred care for TB.[7–10] Traditional models of MDR-/RR-TB care tend to be disease-focused, i.e., focused on diagnosis, drug regimens and culture conversion, emphasising directly observed therapy (DOT) without consideration of the individual needs and circumstances of each patient.[7,11] TB disproportionately affects socio-economically vulnerable populations,[12,13] and patient-centred care aims to incorporate the social, economic, psychological and medical needs of the patient in the decision-making and treatment process, and to be responsive to changes in the patient's needs.[7,8,11]

While patient-centred care is one of the three pillars of the WHO's End TB Strategy,[1] it is not always clear how specific patient needs can be met, what the challenges are in addressing these and what health system strategies are needed to better deliver patient-centred care for TB patients. The aim of the present analysis was to describe the medical, social and geographic circumstances of MDR-/RR-TB patients in South Africa and discuss the implications for service delivery and provision of patient-centred care.

METHODS

This was a retrospective descriptive study utilising data from 195 patients newly diagnosed with MDR-/RR-TB in the third quarter of 2016 in South Africa, which were sampled for a previous study describing the geographic journeys made by these patients in the course of their care.[14] A new treatment episode was defined as having no MDR-/RR-TB laboratory result in the 6 months prior to the diagnosing RR-TB result. A sample of 15 patients was randomly selected from each of the 13 districts across three provinces; four districts each in the Eastern Cape and Western Cape and five districts in KwaZulu-Natal. Laboratory data were collected from the National Health Laboratory Service (NHLS; Pretoria, South Africa) central data warehouse.

The districts were selected to include both rural and urban environments and included areas with care decentralised to various extents, ranging from fully decentralised, where patients could be initiated on treatment at the primary care level, through to a fully centralised model where all patients were required to be admitted at a specialised TB hospital to initiate treatment.[14] Patient demographics and clinical notes on medical and social history were collected by reviewing medical records.

AFFILIATIONS

1 Division of Medical Microbiology, University of Cape Town, Cape Town, South Africa
2 TB Centre, London School of Hygiene & Tropical Medicine, London, UK
3 Health Systems Research Unit, South African Medical Research Council, Cape Town, South Africa
4 Centre for the AIDS Programme of Research in South Africa, Africa Health Research Institute, University of KwaZulu-Natal, Durban, South Africa
5 Africa Health Research Institute, School of Laboratory Medicine & Medical Sciences, College of Health Sciences and School of Public Health, University of the Witwatersrand, Johannesburg, South Africa
6 Institute for Global Health and Development, Queen Margaret University, Edinburgh, Scotland, UK
7 Department of Medical Microbiology, University of KwaZulu-Natal, Durban, South Africa
8 School of Nursing and Public Health, University of KwaZulu-Natal, Durban, South Africa
9 Institute of Infectious Disease and Molecular Medicine and Wellcome Centre for Infectious Diseases Research in Africa, University of Cape Town, Cape Town, South Africa
10 School of Biomedical Sciences, University of Western Australia, Perth, WA, Australia
11 Livingstone Hospital, Eastern Cape Department of Health, Port Elizabeth, South Africa
12 Department of Medicine, University of Cape Town, Cape Town, South Africa

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HIV profiles and health indicators of patients entering care were described using laboratory data from 2 months prior to and 2 months after the MDR-/RR-TB treatment start date. Where MDR-/RR-TB treatment start dates were not available, the date of the first positive RR-TB result was used. Extensively drug-resistant TB (XDR-TB) was defined as TB which is resistant to isoniazid, rifampicin (RIF), fluoroquinolone and a second-line injectable. Pre-XDR-TB was defined as resistance to isoniazid, RIF and either a fluroquinolone or a second-line injectable agent.[15] Anaemia (female: haemoglobin <120 g/L; male: <130 g/L) and body mass index (BMI) (underweight, BMI <18.5 kg/m^2) were categorised based on WHO definitions.[16–18] Hypoalbuminaemia was defined as serum albumin <36 g/L.[19]

Extrapulmonary TB, previous TB episodes (drug-susceptible and MDR-/RR-TB) and comorbidities were determined by medical folder review. Comorbidity data were captured from the folder entries, beginning from the entry into care until 9 months of follow-up. Undated comorbidities were assumed to be present when the patient entered care. Renal impairment was separated into acute and chronic disease by reviewing medical notes and laboratory data (serum creatinine, where available). Advanced HIV disease was defined as a CD4 count <200 cells/mm^3.[20]

Mental health disorders were categorised according to DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition) Axis 2.[21] Social circumstances were recorded based on medical records and receipt of government grants. Government grants are predominantly disability grants; individuals diagnosed with MDR-/RR-TB are eligible for disability grants, although access is not universal.[22] Case studies of individual patients were constructed using both medical records and NHLS data; these were purposively selected to represent some of the different social and medical challenges experienced by patients and illustrate their vulnerabilities. Names used in the case studies are pseudonyms.

Patients' home addresses were obtained from medical records and geolocated using a process of triangulation between ArcGIS 10.7 (ESRI, Redlands, CA, 2017) World Geolocator, Google maps and the national census subplaces shapefile (Statistics South Africa 2011). A street address or nearby landmark was used where possible, or the centre-point of the area in which the patient lived. Home address coordinates were used to calculate the straight-line distance travelled by the patients to the diagnosing facilities, defined as the facility at which the first RR-TB sample was taken, and the treatment-initiating facilities, which were determined by matching laboratory sample dates and MDR-/RR-TB treatment start dates from the folder review. Where no sample was taken on the day of treatment start, a hospital admission date or a known treatment-initiating facility visited closest in time to the start of treatment was used. For 22 geolocated patients with no available treatment start dates, the visit date to the first site visited at which initiation was possible was used.

TABLE 1 Patient demographics and clinical factors at MDR/RR-TB entry into care*

Demographics			*n* (%)
Male			120 (62)
Age, years			
0–19			9 (5)
20–39			109 (56)
40–59			69 (35)
>60			7 (4)
MDR/RR-TB profile			
Resistance profile			
RIF-monoresistant TB			34 (18)
MDR-TB			91 (47)
Pre-XDR-TB			32 (16)
XDR-TB			24 (12)
RR-TB (Xpert only†)			13 (7)
Extra-pulmonary or disseminated TB (recorded)			5 (3)
Previous episode of TB (DS- or MDR/RR-TB) (recorded)			122 (63)
General markers of disease severity		Data available	
Anaemia (females: <12 g/dL; males: 13 g/dL)	130		97 (75)
Hypoalbuminemia (<37 g/L)	104		92 (88)
Underweight (BMI < 18.50 kg/m^2)	69		59 (86)
HIV-positive	194		134 (69)
CD4 <200 cells/mm^3	92		48 (52)
Of which: CD4 50–100 cells/mm^3	92		12 (13)
CD4 0–50 cells/mm^3	92		20 (22)

*For general markers of disease severity, *n* = total number of test results available.
†Some patients were determined to have MDR/RR-TB using Xpert test alone, with no additional drug susceptibility results available from culture or line-probe assays.
MDR-TB = multidrug-resistant TB; RR-TB = rifampicin-resistant TB; RIF = rifampicin; XDR-TB = extensively drug-resistant TB; DS-TB = drug-susceptible TB; BMI = body mass index.

CORRESPONDENCE
Leila Mitrani, Division of Medical Microbiology, UCT Faculty of Health Sciences, Room 5.24, Falmouth Building, Anzio Road, Observatory 7925, South Africa. email: Leila.mitrani.uct@gmail.com

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Data sharing: The data generated by this research contains confidential patient information and cannot be shared publicly; however, the corresponding author may be contacted directly with any such queries.

KEY WORDS
patient complexity; health systems; integrated care

Ethics statement

Ethical approval for this study was obtained from the Human Research Ethics Committee, University of Cape Town, Cape Town, South Africa (HREC 350/2016) and the London School of Hygiene & Tropical Medicine, London, UK (11680). Research approval was granted in all three provinces (EC_2016RP30_232, KZ_2016RP51_466, WC_2016RP45_978).

RESULTS

Among the 195 patients, one patient was found to have been incorrectly diagnosed as having MDR/RR-TB and was excluded from further analysis; 181/194 (93%) medical records were located for the remaining patients. Three patients were found to have a specimen with an RR-TB result taken earlier than the third quarter of 2016 and the new diagnosis date was used. Overall, 62% of patients were male; 56% were aged 20–39 years (Table 1). In total, 18% of patients were diagnosed with RIF mono-resistant TB (RR-TB), 47% had MDR-TB (with confirmed/unknown second-line drug susceptibility), and 16% had pre-XDR-TB and 12% had XDR-TB (Table 1).

HIV

Of the 194 patients, 134 (69%) were HIV-positive; viral loads were available for 68 (51%), 36 (53%) of whom had a viral load of >1000 copies/ml (Figure). CD4 count was available for 92 (69%) HIV-positive patients, 48 (52%) of whom had advanced HIV (CD4 <200 cells/mm^3) and 20 (22%) had CD4 <50 cells/mm^3 (Table 1).

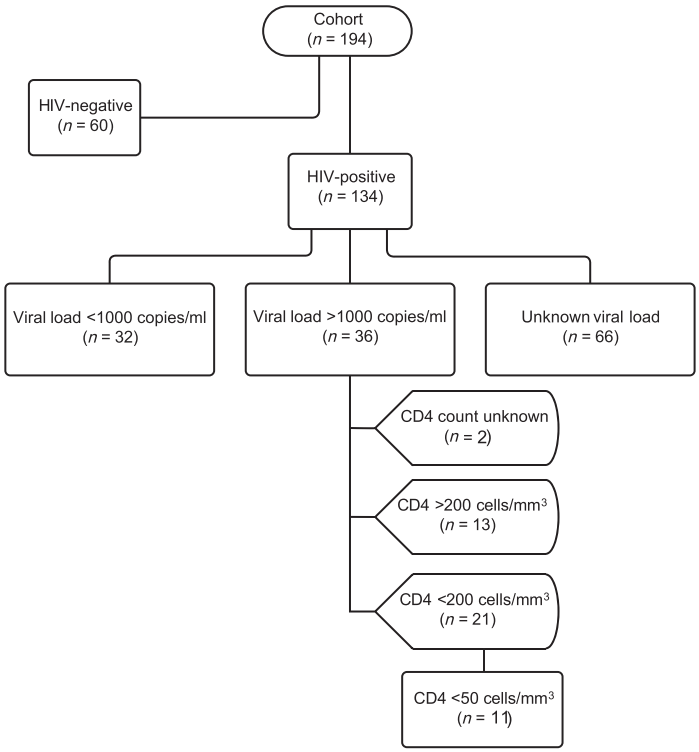

FIGURE Distribution of patients in HIV categories at the start of MDR-/RR-TB treatment. Where treatment start dates were not available, the first positive RR-TB result date was used. CD4 count breakdown shown here only for patients with viral loads >1000 copies/ml. MDR-/RR-TB = multidrug-resistant/rifampicin-resistant TB.

Other comorbidities

While 72 chronic comorbidities were reported, only three were dated after the start of treatment, suggesting that onset predominantly predated MDR/RR-TB diagnosis. Patients presented with, or experienced, a range of acute and chronic comorbidities other than HIV within 9 months of treatment initiation (Table 2). The most common acute comorbidities were infections related to immunocompromise (n = 13), which included cytomegalovirus, cryptococcal meningitis, *Clostridium difficile*, herpes simplex, herpes zoster, *Candida albicans* and other fungal infections. The most common chronic comorbidities were hypertension (n = 13), mental health conditions (n = 11) and diabetes (n = 10). Mental health conditions included mood (n = 5), cognitive (n = 3) and psychotic (n = 2) disorders, and an unspecified disorder (n = 1) (Table 2). Both chronic (n = 8) and acute (n = 6) renal impairment were recorded, with four of the acute episodes being probable anti-TB drug adverse events (all four patients were receiving kanamycin).

Social circumstances

Less than a quarter of patients were recorded as formally employed (n = 44), and only 24 of the remaining 151 patients were recorded to be receiving government grants, indicating a probable high unemployment rate. The level of education was known for 132 patients, 28/132 had received primary-level schooling alone, while two had received tertiary education. Previous incarceration was reported for 28 (14%) patients. Almost a third of patients were recorded to be smokers (n = 58) or misusing alcohol (n = 52) and 17 were recorded to have disclosed substance misuse (usually cannabis, mandrax or crystal methamphetamine).

Patients experienced a range of complex social and medical circumstances that might adversely impact their capacity to initiate or adhere to treatment (Table 3). The most common of these

TABLE 2 Comorbid events present in the first 9 months of treatment

	Comorbid events *n*
Acute conditions	
HIV-associated opportunistic infections	13
Acute infections, other	9
Syphilis	3
Pneumonia	2
Sepsis	2
Pelvic inflammatory disease	1
Colitis	1
Acute condition, other	10
Renal impairment, acute	6
Cardiovascular event	3
Hypoglycaemia	1
Chronic conditions	
Hypertension	13
Mental health condition	11
Diabetes	10
Renal impairment (chronic)	8
Sensory disability (baseline visual/auditory)	6
Malignancy	5
Restrictive and other chronic lung disease	5
Epilepsy	5
Physical mobility impairment	4
Hepatitis B	3
Hyperthyroidism	1

TABLE 3 Social circumstances affecting patients

Social circumstance	*n*
Travelling to health facility to initiate and/or continue treatment	
Physical health impacts capacity to travel	13
Transport challenges associated with costs, distance and access	5
Inflexible employment or fear of loss of employment	4
Factors impacting potential admission to initiate treatment	
Need to care for children	26
Need for concomitant access to mental health services	4
Reliance on traditional medicine	2
General challenges to accessing and completing treatment	
Sick household/family member	17
Unsupportive family circumstances, e.g., family member abusing substances	6
Lack of ID documents to facilitate access to disability grants	3
Homelessness	2
Child-headed households	2

were having child dependents (n = 24) and having ill family members (n = 17) (Table 3). Also notable were difficulties accessing transport to facilities (n = 5) and unsupportive home environments (n = 6), for example, living with a relative misusing substances (Table 3).

Geographic challenges

Patient home addresses were available for 181 (93%) patients and 166 (86%) were successfully geolocated. Among these, 81 were located to an exact address, road or nearby landmark. The remaining 85 were identified to the level of suburb, town, city or rural area. The 166 (86%) geolocated patients were matched to a diagnosing healthcare facility and 154 (79%) were matched to an initiating healthcare facility. The median straight-line distance from a patient's residence to the diagnosing healthcare facility was 2.0 km (range 0–245.3), with 13% estimated to travel more than 20 km. The median distance to the facility initiating treatment was 15.7 km (range 0.1–290.2), with 42% of patients estimated to travel more than 20 km.

Case studies

The case studies presented here (Table 4) show the diverse challenges experienced by individual patients, and the way in which these factors are often inter-linked, multi-layered and complex. Pieter struggled with financial as well as social support making it difficult to alleviate the emotional and financial burden of treatment. Funeka's story highlights the intersection between social and mental health challenges that complicated treatment.

DISCUSSION

This study demonstrates that MDR-/RR-TB patients often present with, or develop, a variety of medical complexities such as advanced HIV disease and poor general health, as well as many other comorbidities, including mobility challenges and mental health conditions. In addition to medical complexity, patients also experienced a range of socio-economic difficulties such as lack of family support, substance misuse or a history of incarceration, and often need to travel long distances to reach healthcare facilities. Taken individually, these factors have the potential to impact a patient's ability to initiate or continue MDR-/RR-TB treatment but, as shown by the case studies, these circumstances do not always occur in isolation and may compound one another.

The HIV-DR-TB coinfection rate of patients in this cohort (69%) was slightly higher but similar to the 59% coinfection rate reported by the WHO for all TB cases in South Africa.[1] It should be noted that a large proportion of HIV-positive patients were virally unsuppressed and had advanced HIV with very low CD4 counts. Although it is not clear from the data whether the high viral loads were due to treatment interruption, virological failure or a patient never having received antiretroviral treatment (ART), all of these scenarios are of concern. In addition to advanced HIV, more than half of all patients had been previously treated for TB and a significant proportion were underweight and had poor general health. The high number (66/134) of patients with unavailable viral load results is likely due to national guidelines, which call for 6–12 monthly testing after ART initiation; this may not always coincide with MDR-/RR-TB diagnosis.[23]

The large proportion of patients presenting with advanced HIV highlights the need to successfully treat and retain HIV-positive patients in care in order to effectively treat MDR-/RR TB. With the higher risk of mortality, treatment of these patients is complex, and often requires a more intensive approach than those with less advanced illness. While there is growing awareness of the need for differentiated care in HIV treatment, a similar model needs to be considered in MDR-/RR-TB care, especially considering the wide variety of comorbidities. Differentiating treatment according to the full spectrum of the patients' needs and integration with HIV care, including integration of dispensed medications for different illnesses, could also reduce the number of visits needed.[24]

TABLE 4 Patient case studies: the medical and social complexity of an MDR/RR-TB patient

Prior to health seeking for the MDR/RR-TB event, Pieter* (33 years, male) spent 7 years in prison. He subsequently began drug-susceptible TB treatment and ART and interrupted both treatments several times. In 2016, he received a positive MDR-TB result and entered MDR/RR-TB care the same month. He resided around 8 km from his diagnosing health care facility and 5 km from the facility where he started RR-TB treatment.

Upon entering care, he was severely underweight, with a high viral load, low CD4 count and HIV nephropathy. He was unemployed and unable to apply for unemployment insurance fund benefits, as his national identification document had been stolen. He was also a cannabis and mandrax user. He started on ART 2 months after commencing MDR-TB treatment and was discharged almost 4 months later, after nearly 6 months' of hospitalisation. Following discharge, his parents did not allow him to return home due to strained relations.

Funeka* (53 years, female) had a bipolar mood disorder at the time of her diagnosis with MDR-TB. She was unemployed, tested HIV-negative and lived around 62 km from her diagnosing health care facility and 129 km from her treatment-initiating facility. The TB clinician felt that she was not adequately medicated for her psychiatric condition at the time of treatment; also, she did not always take her medication consistently. She had uncertain family support, at times accusing her family of stealing from her. Both her husband and her daughter died of TB in the same year as she initiated MDR/RR-TB treatment. She was given a brief leave of absence from the ward but returned to the facility in a manic state. At times, she tried to run away from hospital and frequently displayed violent behaviour.

*Not the patient's real name.
MDR-TB = multidrug-resistant TB; RR-TB = rifampicin-resistant TB; ART = antiretroviral treatment.

The medical vulnerability of patients is further highlighted by the range of other comorbidities present in this cohort. Among these were mental health conditions, which may be present at baseline or develop during illness, have similar risk factors to, and considerable intersection with, TB,[25–28] and which may also be associated with reduced treatment adherence.[26,29] South Africa has limited availability of mental health care resources, and some research recommends training nurses at primary health care level to better identify those who can be managed as outpatients.[30] However, some mental health conditions might still necessitate patients to be treated at higher levels of care in order to access clinical support. The variety of illness profiles presented here make it difficult to develop standardised treatment approaches.

Overall, respectively 13% and 42% of patients resided more than 20 km from the facility at which they were diagnosed and initiated on treatment. These data are comparable to reports in Kwa-Zulu Natal, where XDR-TB patients were 2.9 km from the nearest clinic and 17.6 km from the nearest hospital,[31] although probable travel routes and not, straight-line distances were used in the Kwa-Zulu Natal study. It is likely that distances in this study are underestimated, as real-world routes must circumnavigate land features and therefore, tend to be longer than straight-line distances.

Increased travel distances to health care facilities have been shown to decrease retention in ART,[32,33] and are also problematic in the context of MDR-/RR-TB care.[34] This is likely to be exacerbated if patients must make multiple visits for different health conditions. Even when travel distances are shorter, transport to health facilities can still be problematic, especially in cases of general physical weakness and mobility challenges. The economic cost of TB can be catastrophic for households due to loss of employment and increased nutritional resource and travel costs, further burdening already economically vulnerable patients.[22,35,36] Government-issued social grants, as compensation for the loss of employment associated with prolonged disease, are often difficult for patients to access and may not be available until significant cost has already been incurred.[22,36] This highlights the need for greater patient transport service availability and/or financial assistance towards transport for patients both entering care and receiving follow-up care. Context-specific, innovative approaches to providing outreach services should also be incorporated into service provision.

Unfortunately, there are few studies describing the social context and challenges with either drug-susceptible or drug-resistant TB in a large cohort in South Africa. However, a few studies use in-depth interviews to explore these challenges faced by patients. Studies in Uganda and Eswatini found that home-based care allowed patients and caregivers more time to seek part-time work, care for children and tend livestock.[34,37] In this cohort, many patients had children to care for and several had difficulties initiating treatment or collecting medication due to employment commitments. This highlights the need for flexibility around hospital admission and daily or monthly dispensing of medication.

Other social challenges included substance misuse and a history of incarceration. MDR-/RR-TB is known to be prevalent in correctional facilities,[38] but the social challenges related to seeking treatment, employment and social support post-incarceration may be present and substance abuse is known to negatively affect treatment outcomes.[39] The case studies presented in this study demonstrate how multiple medical and socio-economic complexities may occur concurrently in an individual patient. These may be interrelated, and compound other challenges faced by a patient. These challenges need to be identified and addressed by health care providers, including allied health professionals, such as social workers, to help empower patients, address their needs and make it easier for them to continue treatment.[7,8,40]

CONCLUSION

MDR-/RR-TB patients, described here, are at risk medically, socially and economically, and the intersection between these vulnerabilities problematises a one-size fits all model of treatment. This highlights the need for health care providers and the health care system, to look beyond the purely medical solutions and place greater emphasis on individualising the provision of treatment, to define and deliver a complete package of care, that is differentiated, integrated, responsive and patient-centred.

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OBJECTIF : Décrire les profils médicaux, socioéconomiques et géographiques des patients atteints de TB résistante à la rifampicine (RR-TB) et les implications en matière de soins centrés sur le patient.
CONTEXTE : Treize districts de trois provinces d'Afrique du Sud.
MÉTHODE : Cette étude descriptive a analysé les dossiers médicaux et de laboratoire de 194 patients ayant reçu un diagnostic de RR-TB au troisième trimestre de 2016.
RÉSULTATS : L'âge médian était de 35 ans ; 120/194 (62%) patients étaient des hommes. Un traitement antituberculeux antérieur était documenté chez 122/194 (63%) patients, et 56/194 (29%) avaient une résistance à la fluoroquinolone et/ou à un agent injectable de deuxième ligne documentée. Sur 134 (69%) patients infectés par le VIH, les charges virales étaient disponibles pour 68/134 (51%) patients (36/68 [53%] avaient des charges virales >1 000 copies/ml) et les taux de CD4 étaient disponibles pour 92/134 (69%) patients (20/92 [22%] avaient un taux de CD4 $<$50 cellules/mm^3). Les patients présentaient diverses autres comorbidités, dont hypertension (13/194, 7%) et troubles psychiques (11/194, 6%). Sur les 194 patients, 44 (23%) avaient un emploi. Les autres problèmes socioéconomiques comprenaient la toxicomanie (17/194, 9%) et le fait d'avoir un membre de sa famille malade (17/194, 9%). Respectivement 13% et 42% des patients parcouraient plus de 20 km pour se rendre à leur centre de diagnostic et au centre de soins responsable de l'instauration du traitement.
CONCLUSIONS : Les patients atteints de RR-TB avaient divers problèmes médicaux et sociaux. Ces résultats soulignent le besoin de soins intégrés, différenciés et centrés sur le patient afin de mieux répondre aux besoins spécifiques et aux vulnérabilités sous-jacentes de chaque patient.

Public Health Action (PHA) welcomes the submission of articles on all aspects of operational research, including quality improvements, cost-benefit analysis, ethics, equity, access to services and capacity building, with a focus on relevant areas of public health (e.g. infection control, nutrition, TB, HIV, vaccines, smoking, COVID-19, microbial resistance, outbreaks etc).