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Reasons for defaulting from drug-resistant tuberculosis treatment in Armenia: a quantitative and qualitative study

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SUMMARY

SETTING: Armenia, a country with a high prevalence of drug-resistant tuberculosis (DR-TB).

OBJECTIVE: To identify factors related to default from DR-TB treatment in Yerevan.

DESIGN: Using a retrospective cohort design, we compared defaulters with patients who were cured, completed or failed treatment. Patients who initiated DR-TB treatment from 2005 to 2011 were included in the study. A qualitative survey was conducted including semi-structured interviews with defaulters and focus group discussions with care providers.

RESULTS: Of 381 patients, 193 had achieved treatment success, 24 had died, 51 had failed treatment and 97 had defaulted. The number of drugs to which the patient was resistant at admission (aRR 1.16, 95%CI 1.05–1.27), the rate of treatment interruption based on patient's decision (aRR 1.03, 95%CI 1.02–1.05), the rate of side effects (aRR 1.18, 95%CI 1.09–1.27), and absence of culture conversion during the intensive phase (aRR 0.47, 95%CI 0.31–0.71) were independently associated with default from treatment. In the qualitative study, poor treatment tolerance, a perception that treatment was inefficient, lack of information, incorrect perception of being cured, working factors and behavioural problems were factors related to treatment default.

CONCLUSION: In addition to economic reasons, poor tolerance of and poor response to treatment were the main factors associated with treatment default.

KEY WORDS: tuberculosis; default; resistance

THE BURDEN OF TUBERCULOSIS (TB) is high in the former Soviet Union countries, which also face high levels of drug-resistant tuberculosis (DR-TB).[1,2] Armenia belongs to the 27 countries with a high burden of multidrug-resistant tuberculosis (MDR-TB, defined as *Mycobacterium tuberculosis* resistant to both isoniazid [H, INH] and rifampicin [R, RMP]).[1]

The incidence of new TB cases in Armenia is estimated at 73 per 100 000 population (95% confidence interval [CI] 59–88). MDR-TB accounted for 14.5% (95%CI 1.6–18.0) of all TB cases in 2007.[2,3] Since 2005, Médecins Sans Frontières (MSF) has provided support to the Armenian National Tuberculosis Programme (NTP) in the treatment of DR-TB.

DR-TB is of special concern, as it can undermine efforts to control the TB epidemic.[4,5] Monitoring outcomes of DR-TB treatment is an important aspect of the surveillance activities adopted to control the spread of *M. tuberculosis*-resistant strains and identify weak areas in treatment management.[6] Default, death and treatment failure are usually used as a measure of poor treatment outcome, whereas the number of patients who achieve cure or who complete treatment is used as an indicator of success.[7] Studies on MDR-TB have reported that a large proportion of unsuccessful outcomes are attributable to default and death.[8–10] This is a major problem in the programme in Yerevan, the capital of Armenia, where despite efforts made to ensure adherence to treatment, 24.7% of patients default from treatment and 7.6% die (source: NTP data 2005–2011). Reasons for treatment default among patients with DR-TB should be further considered to enhance adherence to treatment in settings where DR-TB is a public health priority. In the present study, we assessed factors related to treatment default among DR-TB patients receiving care in Yerevan using retrospective analysis of programme data. To strengthen our findings, we also performed a qualitative study to identify patient and health provider beliefs concerning default from DR-TB treatment.

METHODS

Setting

The NTP/MSF DR-TB programme covers the entire city of Yerevan. Treatment regimens are individualised

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based on results of drug susceptibility testing; at least four effective drugs are given for 15–24 months according to World Health Organization (WHO) guidelines.[6] Injectable second-line drugs (kanamycin, capreomycin) are given until 4 months after culture conversion to negative, and for a minimum of 6 months (intensive phase). Patients are hospitalised until they have two sputum-negative culture or smear results (not necessarily throughout the intensive phase). Treatment administration is under direct observation (DOT) throughout the full course of treatment. Patients undergo medical assessments daily during the first month of treatment, weekly until the end of the intensive phase and monthly during the continuation phase, with careful management of adverse events. Psychological and socio-economic support (financial and nutrition support, transport reimbursement) are provided. The programme was approved by the WHO Green Light Committee in 2006.

Quantitative study

Study population

The study included all patients with laboratory-confirmed DR-TB, either MDR-TB or polydrug-resistant TB (PDR-TB, i.e., resistant to more than one first-line drug other than MDR-TB), who initiated treatment from 2005 to 2011.

Definition of exposure

Data were collected in Koch'6, a software programme developed by MSF for the clinical management of patients with DR-TB that is completed routinely for all patients by two trained data clerks. The database did not include any personal information. Variables abstracted included socio-demographic characteristics, history of substance abuse, TB treatment history, clinical and radiographic findings at baseline, bacteriological baseline status and resistance pattern. Treatment information included emergence of co-morbidities and drug side effects, treatment changes and interruptions and adherence to treatment. Treatment adherence was assessed monthly by the ratio of treatment doses received under DOT divided by the number of doses prescribed. Treatment interruptions were defined as interruption of full treatment for at least one day, and were separated by the clinician into interruptions due to side effects or another medical reason and interruptions due to patient's decision (social reasons, refusal, etc.). Treatment changes corresponded to any change in treatment (either dose or full drug) without treatment interruption.

Outcome definitions

Treatment outcomes were assessed based on WHO recommended definitions.[6] A defaulter was defined as a patient who interrupted the full course of treatment for at least 2 consecutive months. The default rate was calculated as the total number of patients who defaulted by year of admission divided by the total number of patients initiated on treatment in that year; the most recent cohorts were excluded, as a significant proportion of patients were still on treatment.

Statistical analysis

We compared patients who had defaulted from treatment with those who were cured, completed or had failed treatment. Patients still on treatment, transferred out or who died during treatment were excluded. Characteristics associated with treatment default were assessed using generalised linear models for the binomial family. All variables with $P \leqslant 0.20$ in univariate analysis were included in a multivariable analysis. Data were analysed using Stata v10.1 for Windows (Stata Corp, College Station, TX, USA). Correlation between variables was checked prior to their inclusion in the multivariate analysis. Missing data were not replaced or imputed. The main interactions were assessed using a level of significance of $P \leqslant 0.05$.

Qualitative study

The qualitative survey included semi-structured interviews of adult patients who had defaulted from DR-TB treatment and focus group discussions with health care workers and pychosocial support teams. We also recorded reasons for stopping treatment, which are routinely collected by the adherence team. All defaulters were traced and invited by telephone to participate in a face-to-face interview outside the DR-TB programme facility with a trained Armenian psychology student who was not involved in the DR-TB programme. Signed informed consent was provided by the patients. Focus group discussions were conducted by an experienced psychologist. The recordings were transcribed in Armenian and translated verbatim into English. To reduce bias during the interview, interviewers were not informed about the study objectives and were trained on how to obtain information without influencing the subject response. Data analyses were performed using an interim analysis process. The major themes were listed according to the objectives of the study before starting the analyses (a priori codes), and were enriched if other themes were found to be relevant to the study objectives (inductive codes). The selected themes were identified in the transcribed text (coding) by a qualitative researcher. The study was conducted in November 2011.

Ethical approval was obtained from the ethics committee of the University of Psychology of Yerevan and the Comité Consultatif de Protection des Personnes, Saint Germain en Laye, France.

RESULTS

Quantitative study

During the study period, 486 patients initiated DR-TB treatment in Yerevan. Of these, 100 were still on

treatment at the time of the study, 193 had achieved treatment success (134 cured, 59 completed), 24 had died, 18 were transferred out, 51 had failed treatment and 97 had defaulted. From 2006 to 2009 the default rate ranged between 22% and 27%. The median duration of treatment for defaulting patients was 6.5 months (interquartile range [IQR] 4.3–12.0). Of the 97 defaulter patients, 69 (71.1%) had defaulted during the intensive phase and 86 (88.7%) while on ambulatory treatment.

Among the socio-demographic factors analysed, being male, having been in prison and alcohol intake were statistically associated with defaulting from treatment. Although previous TB treatment history and outcomes of previous treatment were not associated with default, the number of past courses of antituberculosis treatment was significantly associated with default (Table 1). We found no association with clinical condition at admission; however, smear status, resistance pattern (PDR-TB vs. MDR-TB) and the number of drugs to which the patient was resistant were significantly associated with default (Table 2). The number of treatment changes and treatment interruptions (due to patient decision and side effects) per year of treatment, the monthly treatment adherence rate and the annual rate of side effects were significantly associated with treatment default. Patients who culture-converted during the intensive phase were less likely to default (Table 3).

In the multivariate analysis, the number of drugs to which the patient was resistant at admission, the rate of treatment interruption based on the patient's decision and on side effects and the absence of culture conversion during the intensive phase of the treatment were independently associated with defaulting from treatment (Table 4). An analysis including only MDR-TB patients showed similar results (data not shown).

Findings of the qualitative study

Of 97 defaulters reported in the programme records, four were registered twice as having defaulted. Of the 93 patients, only 12 could be interviewed (Figure). All patients interviewed mentioned difficulties in dealing with side effects, and 11 reported side effects as one of the main reasons for defaulting. The second factor most frequently mentioned was fear that the treatment was not effective or even harmful ($n = 9$). Six patients said that they did not think they needed the treatment any longer (they felt better or cured after a few months of treatment or several negative culture

Table 1 Sociodemographic variables associated with defaulting drug-resistant treatment

	No defaulter* *n* (%)	Defaulter *n* (%)	Univariate analysis	
			RR (95%CI)	*P* value
Sex				
Female	59 (24.2)	8 (8.2)	Reference	
Male	185 (75.8)	89 (91.8)	2.72 (1.39–5.33)	0.004
Age, median [IQR]	37 [25–49]	40 [33–48]	1.01 (1.00–1.02)	0.204
Single	99 (41.1)	47 (50.0)	1.29 (0.92–1.82)	0.139
Ex-prisoner	61 (25.0)	37 (38.1)	1.53 (1.09–2.14)	0.013
Unemployed	30 (15.3)	5 (6.8)	0.49 (0.21–1.13)	0.095
Illicit drug user	6 (2.5)	3 (3.1)	1.17 (0.46–3.00)	0.741
Alcohol intake				
None	139 (57.0)	42 (43.3)	Reference	
Moderate	98 (40.2)	49 (50.5)	1.44 (1.01–2.04)	0.043
Excessive	7 (2.9)	6 (6.2)	1.99 (1.04–3.79)	0.036
Type of patient				
New	48 (19.7)	19 (19.6)	Reference	
Previously treated	196 (80.3)	78 (80.4)	1.00 (0.66–1.53)	0.986
Previous anti-tuberculosis treatment outcomes				
Successfully completed all previous courses of treatment	14 (6.2)	5 (5.5)	0.91 (0.42–1.98)	0.822
Previously defaulted at least once	27 (11.9)	14 (15.4)	1.23 (0.77–1.96)	0.386
Previously failed at least once	42 (18.5)	17 (18.7)	1.01 (0.65–1.57)	0.970
Outcome of most recent previous course of treatment				
Treatment success	14 (6.2)	5 (5.5)	Reference	
Failed	42 (18.5)	17 (18.7)	1.09 (0.47–2.57)	0.835
Defaulted	27 (11.9)	14 (15.4)	1.30 (0.55–3.08)	0.555
Other	144 (63.4)	55 (60.4)	1.05 (0.48–2.30)	0.903
Number of previous courses of treatment, median [IQR]	2 [1–2]	2 [1–3]	1.09 (1.00–1.19)	0.051

*Cured, treatment completed or failed.
RR = risk ratio; CI = confidence interval; IQR = interquartile range.

Table 2 Clinical and bacteriological factors associated with defaulting from treatment for drug-resistant tuberculosis

	No default* *n* (%)	Default *n* (%)	Univariate analysis RR (95%CI)	*P* value
BMI, kg/m²				
Underweight (<18.5)	58 (23.8)	25 (25.8)	1.03 (0.70–1.53)	0.866
Normal	146 (59.8)	60 (61.9)	Reference	
Overweight (⩾25)	40 (16.4)	12 (12.4)	0.79 (0.46–1.36)	0.398
Site of disease				
Pulmonary TB	232 (95.1)	93 (95.9)	Reference	
Extra-pulmonary TB	4 (1.6)	1 (1.0)	0.70 (0.12–4.07)	0.690
Both	8 (3.3)	3 (3.1)	0.95 (0.36–2.54)	0.923
Lung cavities				
No cavitation	30 (12.3)	10 (10.3)	Reference	
Unilateral cavitation	143 (58.6)	58 (59.8)	1.15 (0.65–2.06)	0.627
Bilateral cavitation	71 (29.1)	29 (29.9)	1.16 (0.63–2.15)	0.638
Any comorbidity at baseline	64 (26.2)	31 (32.0)	1.22 (0.85–1.73)	0.280
Diabetes	32 (13.1)	7 (7.2)	0.60 (0.30–1.20)	0.152
Smear status at baseline				
Negative	43 (34.1)	6 (15.4)	Reference	
+	25 (19.8)	12 (30.8)	2.65 (1.10–6.40)	0.030
++	21 (16.7)	5 (12.8)	1.57 (0.53–4.66)	0.416
+++	37 (29.4)	16 (41.0)	2.47 (1.05–5.79)	0.038
Resistance pattern				
PDR-TB	77 (36.5)	16 (19.5)	Reference	
MDR-TB/XDR-TB	134 (63.5)	66 (80.5)	1.92 (1.18–3.12)	0.009
Number of drugs to which patients were resistant at baseline, median [IQR]	3 [2–4]	4 [3–5]	1.14 (1.03–1.25)	0.013

*Cured, treatment completed or failed.
RR = risk ratio; CI = confidence interval; BMI = body mass index; TB = tuberculosis; PDR-TB = polydrug-resistant TB; MDR-TB = multidrug-resistant TB; XDR-TB = extensively drug-resistant TB; IQR = interquartile range.

results). Four patients mentioned that the information received on the disease and its treatment was not sufficient or did not target their specific needs (mainly regarding side effects). Five patients reported having more difficulty in adhering to treatment during the ambulatory phase (Table 5).

From the perspective of programme staff, side effects and the lack of information on DR-TB disease and treatment were identified as the main factors associated with defaulting. Some personnel did not feel trained enough to deliver proper messages on DR-TB. They agreed that education should be adapted to the patients' needs and should continue throughout treatment. Most of the personnel agreed that patients complied better during hospitalisation and that discharge to home-based care was a critical period due to social issues or due to DOT during ambulatory treatment. Consumption of alcohol or illicit drugs

Table 3 Treatment related factors associated with default from treatment for drug-resistant tuberculosis

	No default* median [IQR]	Default median [IQR]	Univariate analysis RR (95%CI)	*P* value
Number of treatment changes/year of treatment follow-up	3.3 [1.6–5.6]	4.8 [2.3–9.0]	1.08 (1.05–1.11)	<0.001
Number of treatment interruptions based on patient decisions/year of treatment follow-up	4.5 [1.2–11.8]	11.9 [5.5–19.1]	1.03 (1.02–1.04)	<0.001
Number of treatment interruptions due to medical decisions other than side effects/year of treatment	0.0 [0.0–1.0]	0.0 [0.0–0.9]	1.12 (1.01–1.24)	0.030
Number of treatment interruptions due to side effects/year of treatment	0.0 [0.0–0.7]	0.0 [0.0–0.9]	1.12 (1.02–1.24)	0.019
Number of side effects/year of treatment follow-up	1.1 [0.0–1.2]	1.8 [0.0–3.1]	1.32 (1.24–1.42)	<0.001
Culture converted during intensive phase of treatment, *n* (%)	123 (52.1)	25 (26.0)	0.44 (0.29–0.65)	<0.001
Time to culture conversion, months	3.3 [1.9–6.3]	3.7 [2.0–8.5]	1.00 (1.00–1.00)	0.232

*Cured, treatment completed or failed.
IQR = interquartile range; RR = risk ratio; CI = confidence interval.

Table 4 Multivariate analysis of factors associated with defaulting from treatment for drug-resistant tuberculosis*

	Multivariate	
	aRR (95%CI)	*P* value
Male sex	2.14 (1.00–4.61)	0.051
Number of drugs to which resistant	1.16 (1.05–1.27)	0.004
Number of treatment interruptions based on patient decision/year on treatment	1.03 (1.02–1.05)	<0.001
Number of side effects/year on treatment	1.18 (1.09–1.27)	<0.001
Culture conversion during intensive phase of treatment	0.47 (0.31–0.71)	<0.001

*The variables included in the final model were those that contributed significantly to improving its likelihood.
aRR = adjusted risk ratio; CI = confidence interval.

and the long duration of treatment were also cited as factors related with defaulting (Table 6). Finally, the definition of treatment failure was debated: there was a perception that some patients were failing treatment but defaulted before being classified as failures.

The following reasons for not returning for treatment were recorded by the adherence team: 21 (24.4%) return to work (10 of whom left the country), 20 (23.3%) behavioural problems (mainly substance abuse), 15 (17.4%) lack of belief in treatment benefits, 10 (11.6%) side effects, 8 (9.3%) comorbidities, 7 (8.1%) feeling healthy, and 3 (3.5%) complex social situation. For 11 patients, the reason was not noted.

DISCUSSION

Our study showed that patients with poor treatment tolerance, based on the number of side effects, and patients with poor treatment response, based on the absence of culture conversion during intensive phase, were at higher risk of defaulting from treatment. This was consistent in both the quantitative and qualitative analyses in the study. Whereas the number of drugs to which the patient was resistant at baseline was an independent predictor of defaulting from treatment, there was no association with the extent and severity of the disease or sputum smear microscopy results at treatment initiation.

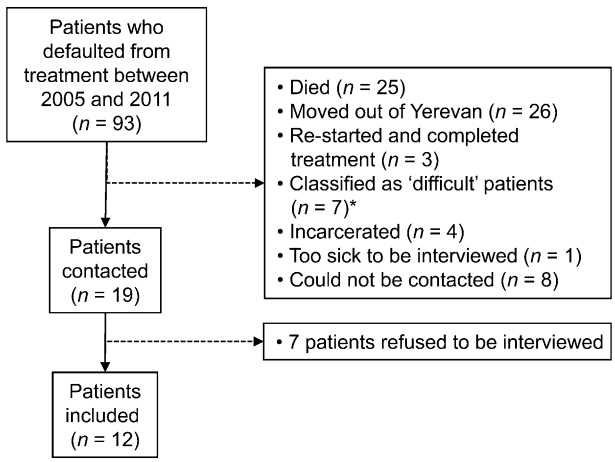

Figure Patient follow-up for qualitative study. *Patients whom the interviewers were advised by the team not to visit at home.

Table 5 Findings of the patients' individual interview (verbatim)

Major themes	Transcribed text
Poor treatment tolerability	I almost died because of one drug . . . I was getting worse because of that capsules . . . I didn't go anymore to the polyclinic because the side effects were too strong . . . I felt very well myself when I stopped . . . When I was taking the drugs, I was dying . . . My arms were aching a lot, I had dizziness . . . I have stopped and I feel much better . . . Otherwise [if I had not felt better] I had been taking, I had not refused . . . After my nervous system mixed up . . . I had nausea. . . . That's why I was forced to refuse. I took fewer drugs, but the effect was terrible. Better I die than going again through all this. . . . I felt I was dying because of prothionamide . . . because of cycloserine, I was having hallucinations . . . I had ulcer due to PAS . . . I didn't want to continue. As soon as I had the injection I was feeling very bad. . . . First of all you have terrible nausea, and you are awfully weak . . . But for example the day off, . . . I was feeling good. . . . I was feeling bad after the drugs, no other reason [for defaulting]
Treatment not effective or even harmful	All my friends who took the drugs are dead. And me, I am not going to die. I saw people dying in front of my eyes; they were changed, completely different. If I continued my treatment they would have taken me dead outside of my ward . . . Every day there was one who died. That's why we have escaped from there I have been taking so many drugs, so many X-rays were done, they did much and we had no results. I don't know how much influenced those drugs on the lungs. They said that I had to continue the treatment up to 24 months. They said that nobody can guarantee that it will not be repeated.
Feeling better or cured	I was feeling better so I stopped. I didn't want to continue, I was cured. When I interrupted my treatment, I was thinking I was cured.
Lack of specific information	Since I restarted my treatment, nobody provided information about the treatment; they thought I knew everything already.
Difficulties during the out-patient phase of the treatment	It's a difficult moment while passing from one to the other [hospital to ambulatory care]. In the hospital you were not getting crazy and you could eat after the drugs. When I was going to take my drugs (in the polyclinic) I was feeling bad. I took my drugs for about 1 month and I didn't go any more to the polyclinic, since the side effects were too strong and I was getting worse.
Defaulting due to other factors: social issues, duration of treatment, etc.	I tolerated badly the treatment but that was not the reason for defaulting, I had to take care of one of my relatives who was sick. It is an unbearable treatment. How you can take drugs for 3 years?

Table 6 Findings of the focus group discussion with programme staff (verbatim)

Major themes	Transcribed text
Poor treatment tolerability	It is difficult to tell the patients to continue the treatment when they suffer nausea and vomiting. It is very hard to explain that the drugs we provide and makes them feel sick are curing them. The treatment is very long and difficult and the drugs have a lot of side effects, this is a general reason for defaulting for all the patients.
Lack of specific information	The education is enough; even too much information, but we always wonder how much the patient understands. First of all we [should] talk to the patient and we [should] find the level, then adapt [the message] to that level. At the beginning the patient is given information, but during the treatment the patient needs more information from the medical team, about results, about changing drugs (regimen). Most of the time the patients don't know why they have one result like that and why the drugs are changed. Educational work has to be done on permanent basis, the patient needs to know about disease, side effects.
Difficulties during the out-patient phase of treatment	. . . the difficult part is when they go out of hospital. At hospital adherence is good, the patient defaults in the ambulatory phase. The ambulatory is doing too much defaulters . . . In in-patient, defaulting is less.
Consumption of alcohol or illicit drugs	There is one factor with defaulter: narcotic drugs and alcohol. If the patient is a drug user or alcoholic, this is a factor of having defaulters. And also we have a group of patients with whom alcohol and drug abuse is preventing us to work with them.
Defaulting due to other factors: feeling already cured, duration of treatment	The patient is not feeling the difference. They think they are already cured. Two years of treatment is unbearable. The treatment is very long.

To our knowledge, only three studies have looked at factors related to default from DR-TB treatment. Holtz et al. found that treatment default was mostly associated with substance use, dissatisfaction with health care worker attitudes and low socio-economic status.[11] Gler et al. reported that patients receiving a greater number of drugs during treatment were at higher risk of defaulting, while treatment decentralisation after culture conversion had a protective role.[12] In the same study, patient mobility and migration were associated with treatment default. Franke et al. found that treatment default was predicted by substance use and substandard housing conditions.[13] In the latter two studies, the role of side effects was not included in the statistical model. These studies were performed in a context very different to Armenia, i.e., South Africa,[11] Philippines[12] and Peru.[13]

The role of side effects on treatment adherence has been discussed previously for drug-susceptible TB and other diseases that require long-term treatment, such as human immunodeficiency virus/acquired immunedeficiency syndrome.[14–20] The treatment of DR-TB is known to cause frequent severe side effects.[21–23] In the project in Yerevan, free, good quality monitoring and management of side effects was provided thanks to MSF support. Nonetheless, patients and staff agreed that better information about side effects could help patients to tolerate treatment. This is consistent with the finding of a recent meta-analysis that showed that patient education was one of the most effective interventions for reducing default in DR-TB.[24] Engaging community health workers as DOT providers in ambulatory treatment was also highlighted as an important intervention.[24] Education could be particularly beneficial during the out-patient phase of treatment. The first months of the out-patient phase were identified as a sensitive period for treatment adherence. Potential explanations were the loss of trust in the need for treatment during the ambulatory phase, the incorrect belief of being cured once discharged from the hospital, the perception of obtaining less support for the management of side effects and the lack of health education. On the other hand, patients whose clinical or bacteriological condition does not improve during hospitalisation may lose faith in treatment and decide not to continue, as supported by the findings of our quantitative study.

The relationship between sex and default, shown previously for drug-susceptible TB,[15,25–28] was close to significance. This association may be explained by the fact that in Armenia males are more likely to work outside the home; presumably, once their health improves they seek employment, sometimes outside the country. Going back to work was one of the main reasons for treatment default reported by the adherence team. Furthermore, 14.5% of Armenian families have a family member who is a migrant worker, usually male, and mostly in the Russian Federation (93.0%).[29] A recent study showed that 13.9% of migrant workers receiving ambulatory anti-tuberculosis treatment did not complete treatment.[29] Substance abuse is another factor that can explain the association between male sex and defaulting.[30]

Patients' behavioural reasons were also reported by the programme adherence team as a reason for defaulting from treatment. In Armenia, 28% of patients are ex-prisoners, half are regular alcohol consumers and almost 5% are users of illicit drugs (NTP/MSF programme data), all conditions that can make treatment adherence difficult.[14,31,32] It has been proposed that interventions to treat substance abuse during anti-tuberculosis treatment might improve treatment outcomes.[14]

Staff perception that some defaulters were failing treatment needs further assessment. In a study in Peru,

authors re-assessed MDR-TB treatment outcomes using culture results according to WHO definitions. They showed a poor concordance with outcomes reported by the programme.[33] Even with a very good recording system, with the current WHO definitions, treatment failures are identified late, and some true failures are defaulting before being classified as failures.[7] The WHO has now revised the definition of treatment failure, allowing a patient to be classified as such much earlier.[34]

One of the main limitations of the study is the use of a retrospective cohort design based on programme data, which may have affected the quality of data recording. It also prevented a deeper assessment of the role of the social determinants of treatment adherence. Due to the difficulty in tracing patients who had defaulted a long time ago, only a small proportion of defaulters could be interviewed, and these may not be representative of all defaulters of the DR-TB programme. Nonetheless, the findings of the qualitative survey support the results of the quantitative study. Unfortunately, due to the study design, we could not analyse the possible impact of adherence-promoting interventions, such as food support.

In conclusion, our study found that the risk of defaulting from DR-TB treatment in Yerevan was mainly linked to poor treatment tolerability and effectiveness and to the social determinants of the patients. The advent of new anti-tuberculosis drugs such as delamanid and bedaquiline should allow the development of more effective, better tolerated and shorter treatment regimens for DR-TB, which would also improve treatment adherence.[35–38] In addition, reinforced communication, with closer and regular contact between health services and the patient, including substance abuse treatment, during the out-patient phase should help reduce default rates.

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RÉSUMÉ

CONTEXTE : Arménie, un pays à forte prévalence de tuberculose résistante aux médicaments (TB-DR).

OBJECTIF : Identifier les facteurs associés à l'abandon du traitement TB-DR à Yerevan.

MÉTHODES : Nous avons mené une étude de cohorte rétrospective pour comparer les patients ayant abandonné leur traitement aux patients ayant complété leur traitement (guéris, ayant terminés leur traitement ou en échec thérapeutique). Les patients ayant initié leur traitement TB-DR entre 2005 et 2011 ont été inclus. Une enquête qualitative comprenant un entretien semi-directif avec les patients ayant abandonné leur traitement et un groupe de discussion avec les professionnels de santé a été conduite.

RÉSULTATS : Parmi les 381 patients inclus, 193 ont eu un succès thérapeutique, 24 sont décédés, 51 ont eu un échec thérapeutique et 97 ont abandonné leur traitement. Le nombre de médicaments auxquels le patient était résistant à l'initiation (aRR 1,16 ; IC95% 1,05–1,27), le taux des interruptions dues au patient (aRR 1,03 ; IC95% 1,02–1,05), le taux des effets secondaires (aRR 1,18 ; IC95% 1,09–1,27) et l'absence de conversion de culture durant la phase intensive (aRR 0,47 ; IC95% 0,31–0,71) étaient indépendamment associés au risque d'abandon de traitement. L'étude qualitative montrait qu'une faible tolérance au traitement, une perception d'inefficacité du traitement, un manque d'information, un sentiment erroné d'être guéri, des facteurs liés au travail et à des problèmes de comportement étaient liés à l'abandon de traitement.

CONCLUSION : En plus des raisons économiques, la faible tolérance et la faible réponse au traitement étaient les principaux facteurs associés à l'abandon de traitement.

RESUMEN

MARCO DE REFERENCIA: Armenia, un país con alta prevalencia de tuberculosis farmacorresistente (TB-DR).

OBJETIVO: Determinar los factores que se relacionan con el abandono del tratamiento en los casos de TB-DR en Ereván.

MÉTODOS: Se compararon los pacientes que abandonaron el tratamiento con los pacientes que alcanzaron la curación, completaron el tratamiento o tuvieron un fracaso terapéutico, mediante métodos de análisis retrospectivo de cohortes. Se incluyeron los pacientes que iniciaron el tratamiento de la TB-DR entre el 2005 y el 2011. Se llevó a cabo una encuesta cualitativa que comportó entrevistas semiestructuradas a los pacientes que abandonaron el tratamiento e intercambios en grupos de opinión con los profesionales de salud.

RESULTADOS: De los 381 pacientes, 193 alcanzaron el éxito terapéutico, 24 fallecieron, 51 presentaron un fracaso terapéutico y 97 abandonaron el tratamiento. Se revelaron como factores asociados de manera independiente con el abandono del tratamiento: el número de medicamentos a los cuales presentaba resistencia cada paciente en el momento de la hospitalización (cociente de riesgos ajustado [aRR] 1,16; IC95% 1,05–1,27), la tasa de interrupción del tratamiento por decisión del paciente (aRR 1,03; IC95% 1,02–1,05), la tasa de efectos adversos (aRR 1,18; IC95% 1,09–1,27) y la falta de conversión del cultivo durante la fase intensiva (aRR 0,47; IC95% 0,31–0,71). En la parte cualitativa del estudio, los factores que se asociaron con el abandono fueron los siguientes: la tolerabilidad del tratamiento, la percepción de ineficacia terapéutica, la falta de información, la sensación equivocada de estar curado, los factores laborales y los problemas del comportamiento.

CONCLUSIÓN: Además de las razones económicas, la mala tolerabilidad del régimen terapéutico y la escasa respuesta al mismo fueron los principales factores asociados con el abandono del tratamiento.