



Tuberculosis among migrants in Bishkek, the capital of the Kyrgyz Republic

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<http://dx.doi.org/10.5588/pha.17.0002>

Setting: Twenty-two first-line, two second-line and one tertiary health facility in Bishkek, the capital of Kyrgyzstan.

Objectives: Among migrants, a marginalised population at risk for acquiring and transmitting tuberculosis (TB), we determined the proportion with TB among all registered TB cases. For those registered at primary-level facilities, we then reported on their demographic and clinical profiles and TB treatment outcomes.

Design: This was a retrospective cohort analysis of 2012–2013 programme data.

Results: Of 2153 TB patients registered in all health facilities, 969 (45%) were migrants, of whom 454 were registered in first-line facilities. Of these, 27% were cross-border migrants, 50% had infectious TB and 12% had drug-resistant TB. Treatment success was 74% for new cases and 44% for retreatment TB (the World Health Organization target is $\geq 85\%$). Failure in new and retreatment TB patients was respectively 8% and 25%. Twenty-six individuals started on a first-line anti-tuberculosis regimen failed due to multidrug-resistant TB. Eight (25%) of 32 individuals on a retreatment TB regimen also failed. Loss to follow-up was 10% for new and 19% for retreatment TB.

Conclusion: Migrants constituted almost half of all TB patients, drug resistance is prevalent and treatment outcomes unsatisfactory. Fostering inter-country collaboration and prioritising rapid TB diagnostics (Xpert[®] MTB/RIF) and innovative ways forward for improving treatment outcomes is urgent.

Migrants are a vulnerable and often marginalised population at risk of acquiring and transmitting tuberculosis (TB). Migration, whether internal or cross-border, poses a major challenge to TB control in both high- and low-resource countries.^{1,2} This is because migrants encounter challenges in accessing care, and much TB in migrants may remain undiagnosed.^{3–5} Furthermore, those initiating anti-tuberculosis treatment may be unable to complete treatment for various reasons, including change in residence, limited access to longer-term housing, poor socio-economic status and variable access to health care services.^{4–6} These factors contribute to loss to follow-up (LTFU) and death, compromising TB treatment success in migrants. Improving the level of successful TB treatment in this group is an important element in controlling the global TB epidemic. This is of particular concern in the World Health Organization (WHO) European

Region, where both multidrug-resistant (MDR) TB and migration are on the rise.⁷ Finding ways to improve access for hard-to-reach and vulnerable populations, including migrants, is an operational research priority.^{8,9}

Kyrgyzstan is one of the 27 countries with the highest TB and MDR-TB burdens in the world.⁷ It has a large, seasonal and vulnerable migrant population that migrates internally and from neighbouring countries to the capital city of Bishkek. The vulnerability of migrants is accentuated by unfavourable employment conditions, illegal status and barriers to health care access.² This may contribute to treatment-seeking delays, increased disease severity and transmission of MDR-TB.¹⁰ Preventing TB, by stopping the progression from infection to active disease and treating active cases effectively, is also very important for the performance of TB epidemic control.

A PubMed search on TB in migrants revealed no publications on TB programme performance among migrants in Kyrgyzstan or the neighbouring regions. Such information provides a yardstick to guide future TB treatment strategies. Improving TB treatment in migrants is also vital to achieving the global targets for TB control and eventual elimination by the year 2030.⁹

We therefore aimed to report on the proportion of migrants with TB and how well they fared on treatment. Specific objectives were to report on the overall numbers and proportion of migrants registered with TB in all types of health facilities in the capital city of Bishkek. For migrants who were registered at first-line health facilities (family medicine centres), we then reported on 1) their demographic and clinical profile, including the presence of drug resistance; 2) TB treatment outcomes; and 3) the characteristics and factors associated with unsuccessful treatment outcomes.

METHODS

Study design

This was a retrospective cohort study.

Setting

General setting

The Republic of Kyrgyzstan is a small country in Central Asia that borders Kazakhstan, Tajikistan, Uzbekistan and China. Approximately 40% of the 5.8 million population lives in urban areas. Bishkek, the capital and the largest city in Kyrgyzstan, has 874 400 inhabitants. Urbanisation and high natural growth have fos-

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KEY WORDS

operational research; migration; SORT IT; MDR-TB, treatment outcomes

Received 9 January 2017
Accepted 6 June 2017

PHA2017;7(3):218–223
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tered inward economic migration. The economy in Bishkek is primarily agriculture-based, with fruit, vegetables and livestock providing a co-existing system of bartering in the outlying regions.

National Tuberculosis Programme and TB care for migrants

TB management in Kyrgyzstan is in line with WHO guidelines.¹¹ The National TB Programme (NTP) is funded from the national budget and supported by international donors, including the Global Fund (Geneva, Switzerland). TB control interventions are delivered through a network of dedicated TB diagnostic and care facilities. These include TB hospitals and family medicine centres (primary polyclinic services). The family medicine centres are considered the first-line facilities for all patients, including those with presumptive TB. In 2012, 25 facilities in Bishkek were offering sputum smear microscopy services and TB treatment; of these, four have in-patient departments to provide treatment during the intensive phase. Bishkek has one TB reference laboratory where culture and drug susceptibility testing (DST) are performed.

Patients with presumptive TB (formerly called TB suspects) are diagnosed in the health facility where they present (if diagnostic facilities are available) or are referred to centralised sites for diagnosis, following which the results are sent back to the referring facility. Once a patient is confirmed as having TB, he or she is referred to a TB physician and entered into the TB treatment register to start treatment. All new and retreatment TB patients in 2012 were started on standardised TB treatment regimens and had sputum specimens taken for culture and DST. If the results, which become available in about 6 weeks, revealed MDR-TB, patients were switched to an MDR-TB regimen.

From 2013, the Xpert® MTB/RIF assay (Cepheid Inc, Sunnyvale, CA, USA) became available in Kyrgyzstan. All migrants are supposed to receive this test before starting anti-tuberculosis treatment. Xpert is a fully automated nucleic acid amplification test for use with sputum and other specimens. The results are available in 2 hours.¹² If a migrant undergoes Xpert testing and rifampicin resistance is found, the patient is started empirically on MDR-TB treatment (DOTS-plus) while awaiting the DST results, after which the regimen is individualised.

A TB migrant is defined as a person who was diagnosed with TB within 6 months of arrival in Bishkek. Those who arrived from other countries are defined as cross-border migrants, whereas all migrants coming from different regions within the Kyrgyz Republic are termed internal migrants. This information is recorded in the patient cards and TB registers; the definitions are in accordance with the Kyrgyzstan Ministry of Health recommendations.

Anti-tuberculosis treatment is provided free of charge for residents. For non-residents, there is no standardised regulation, and payment decisions are a prerogative of the given health facility.

Study population

The study population included all patients with TB designated as migrants and notified over the period 2012–2013 in Bishkek city.

Study sites

The study sites included all health facilities that register TB in Bishkek city: 22 first-line facilities, two second-line facilities and one tertiary facility.

Data collection, sources and analysis

Aggregate data on the total number of TB migrants registered in the health facilities during 2012–2013 in Bishkek were sourced from the annual TB reports. The data on the clinical characteristics of TB migrants presenting to first-line health facilities (family medicine centres) were obtained from the TB treatment master cards (TB-01), and the hospital TB registers.

The data in the treatment cards were cross-verified with the hospital TB treatment registers. The TB treatment outcomes were standardised in line with WHO guidelines,¹³ and included cured, treatment completed, died, lost to follow-up, transferred out, stopped, failure and not recorded. A failure case was defined as any patient who was started empirically on new (short-course) or retreatment TB drug regimens while awaiting laboratory DST and was then found to have drug resistance.

Measures of risk were estimated using relative risks (RR) and were adjusted using log binomial regression. All available variables including sex, age groups, marital status, employment, TB category, TB type, drug resistance and type of migrant were assessed for crude relative risks. A pre-determined *P* value cut-off of 0.2 was used to select variables to be initially included in the regression model, after which a step-wise backward elimination approach was used to determine the variables that remained significant after adjustment. *P* ≤ 0.05 was considered significant and 95% confidence intervals (CI) were used throughout. Data were entered into Microsoft Excel (v. 2010, Microsoft Corp, Redmond, WA, USA) and analysed using Stata v. 12 (StataCorp, College Station, TX, USA).

Ethics approval

Permission for the study was obtained from the national ethics committee of the Ministry of Health of Kyrgyzstan (Bishkek) and the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease (Paris, France).

RESULTS

Migrants with TB among all registered TB cases in Bishkek

Of a total of 2153 registered TB patients in all health facilities in Bishkek, 969 (45%) were migrants.

Migrants with TB registered in first-line facilities

Of the 969 migrants with TB reported in all health facilities in Bishkek, 454 (47%) were registered at first-line facilities (family medicine centres). Their sociodemographic and clinical characteristics are shown in Table 1. The great majority were unemployed; 27%

ACKNOWLEDGEMENTS

This research was conducted through the Structured Operational Research and Training Initiative (SORT IT), a global partnership led by the Special Programme for Research and Training in Tropical Diseases at the World Health Organization (WHO/TDR, Geneva, Switzerland). The model is based on a course developed jointly by the International Union Against Tuberculosis and Lung Disease (The Union, Paris, France) and Médecins Sans Frontières (MSF, Geneva, Switzerland). The specific SORT IT programme that resulted in this publication was jointly developed and implemented by the WHO Regional Office for Europe (Copenhagen, Denmark); the Operational Research Unit (LUXOR), MSF (Brussels Operational Centre, Luxembourg); and the Centre for Operational Research, The Union. We are grateful for the support of the WHO Country Office in Astana, Kazakhstan, for their support in hosting the training workshops. We also appreciate the active involvement of the WHO Country Offices and the Ministries of Health in Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan in the selection of candidates for training in operational research and identification of research projects in line with their priorities. The programme was funded by the WHO/TDR and by the United States Agency for International Development (Washington, DC, USA) through a grant managed by WHO/TDR. Additional support was provided by the WHO Regional Office for Europe (Copenhagen, Denmark), the Department for International Development (London, UK) and MSF. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript. Conflicts of interest: none declared.

TABLE 1 Sociodemographic and clinical characteristics of migrants with TB in Bishkek, Kyrgyzstan, 2012–2013

| Characteristic | n (%) |
|-------------------------|----------|
| Total | 454 |
| Sex | |
| Male | 267 (59) |
| Female | 187 (41) |
| Age groups, years | |
| 0–18 | 45 (10) |
| 19–39 | 275 (60) |
| ≥40 | 134 (30) |
| Marital status | |
| Single | 242 (53) |
| Married | 208 (46) |
| Employment | |
| Currently employed | 100 (22) |
| Unemployed | 339 (75) |
| Not recorded | 15 (3) |
| Category of TB | |
| New cases | 422 (93) |
| Retreatment cases | 32 (7) |
| Type of TB | |
| Smear-positive PTB | 229 (50) |
| Smear-negative PTB | 158 (35) |
| EPTB | 67 (15) |
| Drug resistance | |
| Pan-susceptible | 372 (82) |
| Mono- and polyresistant | 20 (4) |
| MDR-TB | 34 (7) |
| Unknown | 26 (6) |
| Type of migrant | |
| Internal | 333 (73) |
| Cross-border | 122 (27) |

TB = tuberculosis; PTB = pulmonary tuberculosis; EPTB = extra-pulmonary TB; MDR-TB = multidrug-resistant tuberculosis.

were cross-border migrants. Of all the TB cases at the first-line facilities ($n = 454$), 50% had infectious smear-positive TB, 7% had retreatment TB and 12% had drug-resistant TB (7% of whom had MDR-TB).

TB treatment outcomes

Table 2 shows the treatment outcomes stratified by the type of TB category of the 454 migrants registered at the first-line facilities. Treatment success was 74% for new cases and 44% for retreatment cases, far below the WHO desired target of ≥85%.

The failure rate in new TB cases was 8%, while in retreatment cases it was 25%. LTFU was also high, at respectively 10% and 19% for new TB and retreatment TB.

Twenty-six individuals started on a first-line (short-course) TB regimen were found to have MDR-TB when the DST results were received. These cases were then declared as failures and shifted to an MDR-TB regimen. Similarly, 8 (25%) of 32 individuals started on the retreatment TB regimen were found to have MDR-TB following DST. These individuals were also declared as failures and then switched to an MDR-TB regimen.

Table 3 shows the characteristics of individuals with unsuccessful outcomes. Of 454 TB patients started on treatment at first-line health facilities, 128 (28%) had unsuccessful treatment outcomes. Unsuccessful outcomes were associated with being male, single, aged >25 years, pulmonary TB (PTB) and retreatment TB.

DISCUSSION

This first study on TB treatment outcomes among migrants in Kyrgyzstan shows that almost half of all registered TB patients in Bishkek city were migrants. Approximately one third (27%) of the migrants had crossed international borders, and MDR-TB was prevalent in almost one in ten individuals. Treatment success was 74% in new cases and 44% in retreatment cases, far below the desired WHO target of 85%. Unsuccessful treatment outcomes were mostly related to treatment failure and LTFU.

This study stems from a region where both internal and cross-border migration is common. It is likely to be of practical relevance to the WHO's consolidated action plan for improving TB prevention and care in hard-to-reach populations, including migrants.⁸

This study has several policy and practice implications that merit discussion. First, the fact that almost half of all registered TB patients in the study were migrants emphasises the need for the NTP to fully embrace this group as an integral part of TB control. Importantly, improving TB control at national level would depend on how well TB control is addressed in migrants. The fact that half of all migrant TB patients in our study were smear-positive and therefore infectious, including drug-resistant cases, makes this all the more relevant.

A first step to embrace TB care for migrants in Kyrgyzstan is for the NTP to formulate national guidelines that can be used by all levels of the health system.

Second, the treatment success rates of 74% for new TB and 44% for retreatment TB cases compare well with reports from other urban settings.^{15,16} However, as migrants are a high-risk group for both acquiring and transmitting TB, we should be striving for much higher rates of treatment success—better, in fact, than those in the general population.

Third, we observed a relatively high failure rate of 8% in new TB and 25% in retreatment TB cases. One of the main reasons for this is that all diagnosed patients were first placed on standardised treatment regimens while awaiting DST results. When drug resistance was detected, they were then declared as failures and consequently moved to the MDR-TB regimen. The way forward is to offer Xpert as a first-line diagnostic test for all migrants with presumed TB. Those with rifampicin-resistant TB should be placed directly on an MDR-TB regimen while awaiting their DST results. Although this is now the national protocol, we suspect practical problems of access. This merits specific research. Meanwhile,

TABLE 2 Treatment outcomes among migrants with new and retreatment TB, Bishkek, Kyrgyzstan, 2012–2013

| Treatment outcomes | Category of TB | |
|---------------------|--------------------|----------------------|
| | New cases n (%) | Retreatment n (%) |
| Total | 422 | 32 |
| Successful | 312 (74) | 14 (44) |
| Cured | 128 (30) | 2 (6) |
| Treatment completed | 184 (44) | 12 (38) |
| Unsuccessful | 110 (26) | 18 (56) |
| Death | 15 (4) | 2 (6) |
| Failure | 32 (8) | 8 (25) |
| LTFU | 41 (10) | 6 (19) |
| Transferred out | 22 (5) | 2 (6) |

TB = tuberculosis; LTFU = loss to follow up.

TABLE 3 Characteristics of migrants with unsuccessful tuberculosis treatment outcomes at first-line facilities, Bishkek, Kyrgyzstan, 2012–2013

| Characteristic | Total | Unsuccessful outcomes* <i>n</i> (%) | Crude RR (95%CI) | aRR (95%CI) | <i>P</i> value |
|-------------------------|-------|--|------------------|---------------|----------------|
| Total patients | 454 | 128 (28) | | | |
| Sex | | | | | |
| Male | 267 | 94 (35) | 1 [†] | 1 | |
| Female | 187 | 34 (18) | (0.4–0.7) | 0.6 (0.4–0.9) | 0.003 |
| Age group, years | | | | | |
| 0–25 | 177 | 40 (23) | 1 | 1 | |
| >25 | 277 | 88 (32) | 1.4 (1.0–1.9) | 1.6 (1.1–2.2) | 0.01 |
| Marital status | | | | | |
| Married | 208 | 48 (23) | 1 | 1 | |
| Single | 242 | 79 (33) | 1.4 (1.0–1.9) | 1.6 (1.2–2.3) | 0.003 |
| Employment | | | | | |
| Currently employed | 100 | 27 (27) | 1 | | |
| Unemployed | 339 | 94 (28) | 1.0 (0.7–1.5) | | |
| Category TB | | | | | |
| New cases | 422 | 110 (26) | 1 | 1 | |
| Retreatment cases | 32 | 18 (56) | 2.1 (1.5–3.0) | 1.7 (1.3–2.3) | 0.001 |
| Type of TB | | | | | |
| EPTB | 67 | 9 (13) | 1 | 1 | |
| PTB | 387 | 119 (31) | 2.3 (1.2–4.3) | 2.0 (1.1–3.6) | 0.04 |
| Drug resistance | | | | | |
| Pan-susceptible | 372 | 66 (18) | 1 | | |
| Mono- and polyresistant | 20 | 5 (25) | 1.4 (0.5–4.4) | | |
| Type of migrant | | | | | |
| Internal | 332 | 96 (29) | 1 | | |
| Cross-border | 122 | 32 (26) | 0.9 (0.5–1.4) | | |

*A combination of died, lost to follow-up, failure and transferred out.

[†]Reference category.

RR = relative risk; CI = confidence interval; aRR = adjusted RR; TB = tuberculosis; EPTB = extra-pulmonary TB; PTB = pulmonary TB.

greater decentralisation of existing Xpert machines and prioritisation of migrants may need to be considered.

Fourth, we have identified a number of risk factors associated with unfavourable treatment outcomes, including male sex, single status, age > 25 years, retreatment TB cases and PTB. These groups could benefit from focused attention at programme level. Being male, single and aged >25 years may be linked to unfavourable health-seeking behaviour or lower levels of adherence, issues that are linked to migratory status. These two groups might be constantly searching for employment and economic opportunities. Specific qualitative research in this area is merited. The retreatment category of TB and patients with PTB were also identified as risk factors for unsuccessful outcomes. These two groups may have more severe clinical status at presentation. In particular, adherence to treatment in retreatment TB cases is more difficult, as the drug regimen involves injections, which requires patients to be close to health facilities. This may be practically difficult with migrant populations.

Finally, LTFU in both new and retreatment TB cases was high and may be explained by patients having to leave one geographic area for another in search of employment.

Possible ways to address this issue could include the following: 1) informing patients that if they wish to change their geographic area they can do so, and that they would be given a formal referral letter to another health facility to maintain TB treatment. A buffer stock of drugs could be offered as a safety net, and feedback on treatment outcomes should also be communicated to the referring facility. 2) Kyrgyzstan is planning to introduce an online electronic TB register system. The use of formal referral letters be-

tween health facilities, coupled with the introduction of a unique referral identity code, should facilitate information transfer and tracing at national level. This should be combined with increased efforts for patient awareness and empowerment for continued TB care. 3) The issue of ensuring continued care for cross-border TB migrants is more complex and needs greater regional and inter-country collaboration. We call on the WHO, national governments and other stake holders to urgently continue initiatives that can foster such collaboration.¹⁷

The strengths of the study include the following: 1) as all health care facilities involved with TB in Bishkek were included, the findings are thus likely to reflect the operational reality in the urban setting; 2) the focus on first-line health care facilities, which are the first point of contact with the health system, provides a good yardstick of the basic quality of TB care being offered to migrants; and 3) the study adhered to the Strengthening The Reporting of OBServational studies in Epidemiology (STROBE) guidelines on the reporting of operational research.¹⁴

A limitation of the study is that we used the definition of 'migrant' as recommended in Kyrgyzstan, which may not necessarily be the same for other countries in the region. Reaching agreement on a standardised definition of a TB migrant for all countries in Central Asia would seem a logical step and a priority to allow geographic comparisons in the region. Another limitation is that we did not include second-line and tertiary health facilities in our assessment of treatment outcomes. Our findings may thus reflect a 'best case' scenario. Third, our database did not contain specific information on whether patients with drug resistance were offered Xpert testing. This should be included in the data-

base, as it would permit a good measure of the access to this rapid test. Finally, we were unable to compare the risk factors associated with poor outcomes in the region due to a paucity of published literature.

In conclusion, we have highlighted several possible ways of improving the quality of TB care for migrants. In a part of the world where drug-resistant TB is a major public health problem, making significant strides towards improving TB control for migrants is vital.

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Contexte : Vingt-deux structures de santé de premier niveau, deux de second niveau et une de troisième niveau à Bichkek, la capitale du Kirghizstan.

Objectifs : Parmi les migrants qui sont une population marginalisée à risque d'acquérir et de transmettre la tuberculose (TB), nous avons déterminé la proportion de migrants atteints de TB parmi tous les cas de TB enregistrés. Pour ceux enregistrés dans des structures de premier niveau, nous exposons leur profil démographique et clinique et les résultats du traitement de la TB.

Schéma : Une analyse rétrospective de cohorte des données du programme de 2012 à 2013.

Résultats : Sur 2153 patients TB enregistrés dans toutes les structures de santé, 969 (45%) ont été des migrants ; 454 ont été enregistrés dans des structures de premier niveau. Parmi ces derniers, 27% étaient des migrants transfrontaliers, 50% avaient une TB contagieuse et 12%

avaient une TB pharmacorésistante. Le taux de succès a été de 74% pour les cas nouveaux et de 44% pour les TB en retraitement (cible de l'Organisation Mondiale de la Santé $\geq 85\%$). Les échecs dans les cas nouveaux et les cas en retraitement ont été respectivement de 8% et de 25%. Vingt-six individus mis sous protocole de traitement de TB de première ligne ont eu un échec dû à une TB multirésistante. Huit (25%) des 32 individus en protocole de retraitement de TB ont également eu un échec. Les taux de perdus de vue ont été de 10% pour les cas nouveaux et de 19% pour les TB en retraitement.

Conclusion : Les migrants ont constitué près de la moitié de tous les patients TB, la pharmacorésistance a été prévalent et les résultats du traitement ne sont pas satisfaisants. Il est urgent d'encourager la collaboration entre les pays, de prioriser les diagnostics rapides de TB (Xpert® MTB/RIF) et les manières innovantes d'améliorer les résultats du traitement.

Marco de referencia: Veintidós establecimientos de salud de atención primaria, dos establecimientos de atención secundaria y uno de atención terciaria en Bishkek, la capital de Kirguistán.

Objetivos: En los migrantes, una población marginada con riesgo de contraer la tuberculosis (TB) y transmitirla, se determinó la proporción que padecía TB a partir de todos los casos de TB registrados. En los casos notificados por los establecimientos de atención primaria, se analizaron luego sus características demográficas, el aspecto clínico y los desenlaces del tratamiento antituberculoso.

Método: Fue este un análisis retrospectivo de cohortes de datos del programa del 2012 y el 2013.

Resultados: De los 2153 pacientes registrados con diagnóstico de TB en todos los establecimientos de salud, 969 eran migrantes (45%); 454 se registraron en centros de atención primaria. De estos últimos, el 27% correspondió a migrantes transfronterizos, el 50% presentaba TB contagiosa y el 12% padecía TB farmacorresistente.

La tasa de éxito terapéutico en los casos nuevos de tuberculosis fue 74% y en los casos de retratamiento fue 44% (meta de la Organización Mundial de la Salud $\geq 85\%$). El índice de fracaso terapéutico de los casos nuevos fue 8% y el de los casos en retratamiento fue 25%. En 26 personas que iniciaron el tratamiento antituberculoso de primera línea el tratamiento fracasó debido a la TB multirresistente. También fracasó el régimen de retratamiento en ocho de las 32 personas que lo habían recibido (25%). Las pérdidas durante el seguimiento fueron 10% en los casos nuevos y 19% en los casos de retratamiento.

Conclusión: Los migrantes representan cerca de la mitad de todos los casos de TB, la farmacorresistencia es frecuente y alcanzan desenlaces terapéuticos desfavorables. Es urgente promover la colaboración entre los países, dar prioridad a los medios diagnósticos rápidos de la TB (Xpert® MTB/RIF) y encontrar formas innovadoras de progreso que favorezcan mejores desenlaces terapéuticos.