NOTES FROM THE FIELD

Administrative interventions associated with increased initiation on antiretroviral therapy in Irkutsk, Siberia

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A bundle of initiatives to integrate human immunodeficiency virus (HIV) and tuberculosis (TB) services was assessed for the impact on antiretroviral therapy (ART) initiation at a TB referral hospital in Irkutsk, Russian Federation, from February 2014 to December 2015. The ART initiation rates in 166 ART-naïve patients undergoing anti-tuberculosis treatment (34.1% with multidrug or extensively drug-resistant TB) increased significantly from 14 (17%) pre-intervention to 44 (54%) post-intervention ($P < 0.001$). A survey of TB hospital staff identified administrative prioritisation as the most important initiative for increasing ART initiation.

The oblast of Irkutsk, in Siberia, has the highest rate of human immunodeficiency virus (HIV) infection in the Russian Federation, and experienced a rise in tuberculosis (TB) and HIV co-infection incidence from approximately 5 per 100 000 population in 2007 to 26/100 000 in 2014.^{1,2} In other settings where HIV and TB services have been integrated, high rates of treatment success have been achieved, even for multidrug-resistant (MDR) TB.³ Despite the burgeoning TB-HIV co-epidemic in Irkutsk, TB and HIV services have remained largely separated, and TB physicians are unable to prescribe antiretroviral therapy (ART).

In a prospective cohort of HIV-infected patients admitted to the regional referral hospital to start anti-tuberculosis treatment, we observed that very few were being discharged on ART despite prolonged hospitalisation.⁴ A bundle of initiatives was thus introduced to improve ART initiation. This report compares the rates of ART initiation before and after the interventions were introduced.

INTERVENTION

Pre- and post-intervention assessments were conducted among a prospective observational cohort of HIV-infected patients admitted for anti-tuberculosis treatment from February 2014 to December 2015 at the Irkutsk Clinical Tuberculosis Hospital, the regional facility initiating treatment for the majority of TB-HIV patients. The pre-intervention period was February–August 2014, and the post-intervention period was April–December 2015. The bundle of health system initiatives had no additional cost for the patients and

included: 1) tailoring the educational message and timing of visits from the specialist necessary to begin a request to the HIV centre for ART approval, 2) expediting CD4 cell count and viral load testing, and 3) administrative prioritisation of requests for ART from the TB hospital through weekly cohort reviews of all HIV-infected patients.

Ethics approval for the evaluation of the intervention was granted by the Scientific Centre for Family Health and Human Reproduction Problems (Irkutsk, Russian Federation) and the University of Virginia (Charlottesville, Virginia, USA). Patients were considered eligible for inclusion if they tested HIV-positive by immunoassay and confirmatory Western blot, and were initiated on anti-tuberculosis treatment including treatment for MDR-TB and extensively drug-resistant (XDR) TB. Children aged <15 years and prisoners were excluded. Pre-treatment characteristics and history were collected for both groups, as previously reported.⁵

The primary outcomes of interest included the number of ART-naïve patients who were initiated on ART and the number of days to ART initiation from the date of TB diagnosis. Data were prospectively gathered and secondarily updated prior to hospital discharge/transfer or at the time of death or treatment interruption. Interviews by researchers with the heads of the TB wards and hospital departments were facilitated by a structured questionnaire that ranked the relative importance of each initiative within the bundled intervention.

Statistical analyses were performed using IBM SPSS Statistics 23.0 (IBM, Montauk, NY, USA). The proportion of patients initiated on ART was compared using the χ^2 test; for other group comparisons Student's t -test was applied for normally distributed variables, such as age, and the Mann-Whitney U test was used for non-normally distributed variables, such as CD4 cell counts. A two-tailed P value of 0.05 was considered significant.

RESULTS

Of 199 TB-HIV co-infected patients identified during the study period, 166 (83.4%) were ART-naïve. Fifty-five patients (27.6%) had MDR-TB and 13 (6.5%) had XDR-TB. During the pre-intervention period, 84 ART-naïve patients were enrolled with a median CD4 cell count of 137 cells/ μ l (interquartile range [IQR] 39–233) and a median length of hospitalisation of 127

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KEY WORDS

multidrug-resistant tuberculosis; human immunodeficiency virus; ART; Russian Federation

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TABLE 1 Admission demographics, co-morbidities and ART initiation rates at a large TB referral hospital, Irkutsk, Russian Federation, 2014–2015

Characteristic	Pre-intervention <i>n</i> (%)	Post-intervention <i>n</i> (%)	<i>P</i> value
Total	102	97	
Age, years, mean $\pm$ SD	34.2 $\pm$ 6.7	35.9 $\pm$ 6.1	
Male sex, mean	79 (77.5)	58 (59.8)	
CD4, cells/ μ l, median [IQR]	137 [39–233]	70 [28–173]	
HIV viral load, copies/ml, median [IQR]	201 886 [43 000–640 000]	230 000 [34 000–894 000]	
History of imprisonment	29 (28)	18 (19)	
History of IDU	46 (45)	41 (42)	
ART-naïve	84 (82)	82 (85)	
ART-naïve patients, total	84	82	
Started on ART	14 (17)	44 (54)	<0.001
Time to ART initiation, days, median [IQR]	175 [104–281]	67 [47–104]	<0.001

ART = antiretroviral therapy; TB = tuberculosis; SD = standard deviation; IQR = interquartile range; HIV = human immunodeficiency virus; IDU = intravenous drug use.

days (IQR 79–185). In the post-intervention period, 82 ART-naïve patients were enrolled with a median CD4 cell count of 70 cells/ μ l (IQR 28–173) and a median length of hospitalisation of 124 days (IQR 78–190).

ART initiation rates in ART-naïve patients increased significantly from only 14 (17%) during the pre-intervention period to 44 (54%) post-intervention ($P < 0.001$) (Table 1). Excluding those patients who refused ART or who died, 75% (44/59) of post-intervention patients were started on ART. At the same time, time to ART initiation decreased to a median of 67 days (IQR 47–104) from 175 days (IQR 104–281) among pre-intervention patients ($P < 0.001$). Interviews with TB hospital staff identified administrative prioritisation as the most important factor in increasing ART utilisation, with a median response of 4.5 (minimum 4.0–maximum 5.0) on a 5-point agreement scale (Table 2).

DISCUSSION

The challenges of HIV and drug-resistant TB care in Irkutsk are similar to other Eastern European settings where recent studies suggest low rates of ART initiation similar to those in Irkutsk during the pre-intervention period.^{5,6} As is the case in many areas of the Russian Federation, in Irkutsk treatment for MDR-TB and XDR-TB starts at the hospital, which is institutionally and geographically separate from HIV care and ART dispensation. Cur-

rently, an HIV-infected patient must be evaluated by an HIV specialist and recommended for ART before the case is reviewed by a committee at the specialty centre. Furthermore, active injection drug use, common among this co-infected population, has been a relative contraindication for the committee to authorise ART, although the treatment of opioid addiction with replacement therapy such as methadone remains illegal.

All respondents in this small sampling of stakeholders agreed or strongly agreed that training in ART use and the authorisation for TB clinicians to prescribe ART would further hasten ART initiation. While surveying a broader sampling of health care staff may reduce potential bias, in other TB-HIV endemic settings ART is initiated by providers without specialty training.⁷ At a minimum, ART should begin within 8–12 weeks of anti-tuberculosis treatment initiation but as early as 2 weeks in those with CD4 counts of <50 cells/ μ l, in patients with significant debilitation (a low Karnofsky score or bed-ridden) and/or in those with MDR-TB or XDR-TB.⁸ These recommendations will be challenging to meet in Irkutsk if TB clinicians cannot prescribe ART.

Although the hospital cares for the majority of TB-HIV patients initiating treatment in the region, this single-centre study limits the generalisability of the study's findings. The bulk of costs associated with the intervention were for labour re-organisation and task shifting, which favour sustainability, but formal cost analyses were not performed.

TABLE 2 Interview results of heads of hospital wards and department directors ($N = 5$)

Statement	Response,* median (minimum–maximum)
Improving the educational message about ART that was delivered by the specialist to the patient increased ART initiation	4 (3–4)
Reducing the time between the first and subsequent follow-up visits from the specialist to patients with initial hesitation to begin ART increased ART initiation	3 (3–5)
Improving CD4 cell count and viral load testing availability and speed of delivery of those results to the HIV centre increased ART initiation	3.5 (3–5)
Hospital administration prioritising referrals for ART to speed up committee approval at the HIV centre increased ART initiation	4.5 (4–5)
Improved communication between TB hospital and HIV centre increased ART initiation	4 (2–5)
Would giving training and approval for TB doctors to prescribe ART have further impact on increasing ART initiation in patients before they are discharged from the hospital?	5 (4–5)

*Respondents were asked to rank from 1 to 5 their level of agreement with the statement: 5 = strongly agree; 4 = agree, 3 = neither agree nor disagree; 2 = disagree, and 1 = strongly disagree.

ART = antiretroviral therapy; HIV = human immunodeficiency virus; TB = tuberculosis.

CONCLUSIONS

Initiatives aimed at TB-HIV integration were significantly associated with improved ART initiation at a regional referral hospital in Irkutsk, Siberia. While the bundle of initiatives was cumulatively found to be effective, TB clinicians ranked the component of administrative prioritisation as most important. Further operational studies in Irkutsk and similarly co-infected populations in the Russian Federation should focus on TB clinician-prescribed ART and patient-centred models of care that include substance abuse treatment.⁹

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Un ensemble d'initiatives visant à intégrer les services relatifs au virus de l'immunodéficience humaine (VIH) et à la tuberculose (TB) a été évalué en termes d'impact sur la mise en route du traitement antirétroviral (TAR) dans un hôpital de référence de la TB à Irkoutsk, Fédération de Russie, entre février 2014 et décembre 2015. Les taux de mise en route du TAR chez 166 patients n'en ayant jamais reçu et

traités pour TB (34,1% avec une TB multi-résistante ou ultra-résistante) ont significativement augmenté de seulement 14 (17%) avant l'intervention à 44 (54%) après l'intervention ($P < 0,001$). Une enquête auprès du personnel de la TB a identifié la priorisation administrative comme l'initiative la plus importante dans l'augmentation de l'initiation du TAR.

Se evaluó un conjunto de iniciativas encaminadas a integrar los servicios de atención de la infección por el virus de la inmunodeficiencia humana (VIH) y la tuberculosis (TB), con el objeto de determinar la repercusión de la integración sobre el comienzo del tratamiento antirretrovírico (TAR) en el hospital de referencia de la TB de Irkutsk, en la Federación de Rusia, de febrero del 2014 a diciembre del 2015. La tasa de iniciación del TAR en 166 pacientes que nunca lo habían recibido y que estaban

en curso de tratamiento antituberculoso (34,1% con TB multirresistente o extremadamente multirresistente) aumentó de manera significativa de solo 14 pacientes antes de la intervención (17%) a 44 pacientes después de la misma (54%; $P < 0,001$). Al interrogar al personal encargado de la TB en este hospital de referencia, se puso en evidencia que la priorización administrativa del TAR constituía la iniciativa de más había influido en el incremento de su utilización.