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Systematic case finding for tuberculosis in HIV-infected people who inject drugs: experience from Pakistan

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SUMMARY

SETTING: Pakistan is a high tuberculosis (TB) burden country, moving from low human immunodeficiency virus (HIV) prevalence to a concentrated epidemic driven primarily by people who inject drugs (PWID). The Antiretroviral Treatment Adherence Unit (AAU) in Islamabad, Pakistan, is a residential facility that offers combined treatment for opioid dependence and HIV.

OBJECTIVE AND DESIGN: This retrospective study was conducted to assess TB prevalence among HIV-infected PWID referred to the AAU and to evaluate the diagnostic value of cough as a screening symptom. A single sputum sample was collected regardless of symptoms, and examined using smear, Xpert® MTB/RIF and culture.

RESULTS: Of 888 PWID, 71.5% submitted a sputum sample. More TB cases were detected using Xpert ($n = 25$) than with smear ($n = 10$) or culture ($n = 20$). A TB prevalence of 6141 per 100 000 was estimated based on seven cases already identified as being on anti-tuberculosis treatment and 32 newly diagnosed bacteriologically confirmed TB cases. Both cough and smoking ($\geqslant 10$ pack-years) were associated with increased TB prevalence. Only half of the TB cases reported cough. Rifampicin resistance was reported among 10% (3/29) of newly identified cases.

CONCLUSION: TB prevalence in HIV-infected PWID was 15 times higher than in the general adult population. As a screening symptom, cough has low diagnostic value.

KEY WORDS: PLHIV; Xpert; TB-HIV co-infection; symptom screening

PAKISTAN RANKS FIFTH among high tuberculosis (TB) burden countries, with an estimated prevalence of bacteriologically positive TB of 398 (95% confidence interval [CI] 333–463) per 100 000 population aged >15 years.[1,2] Although the estimated human immunodeficiency virus (HIV) prevalence in the general population is low (0.1%), Pakistan is shifting from a low-prevalence, high-risk country to one with a concentrated epidemic that is mainly driven by two key population groups: people who inject drugs (PWID) and sex workers.

Currently, there are approximately 105 000 PWID in Pakistan, and the estimated HIV prevalence is reported to have risen from 10.8% in 2005 to 27% (weighted prevalence of 37.8%) in 2011.[3–7] Drug users remain at high risk of tuberculous infection and TB disease, and injection drug use is an important factor in HIV-associated TB epidemics worldwide.[8–10] The increased risk is partly due to both the physiological effects of drugs, especially opiates, in terms of compromised immunity, and the environmental and behavioural characteristics of drug users, including tobacco and alcohol use, incarceration and comorbidities such as hepatitis B and C viral infection.[11] Opiates have been shown to reduce the frequency and severity of cough,[12] which is a feature of symptomatic screening in the diagnosis of TB.[13] The effects of drug use can also mean that users have limited access to health services for the diagnosis and treatment of TB, and those who are able to access health care may have difficulty adhering to lengthy anti-tuberculosis treatment regimens.[14]

According to the World Health Organization (WHO) policy on collaborative TB-HIV activities, HIV infection among TB patients, and active TB disease among all people living with HIV (PLHIV), should be monitored in all countries, regardless of the HIV and TB prevalence rates in adults.[15] PLHIV should be systematically screened for active TB at each visit to a health facility for early diagnosis.[16,17] The Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA, USA), a more sensitive diagnostic tool than smear microscopy, is recommended as the front-line tool for the diagnosis of TB.[10,16]

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This retrospective study was aimed to determine TB prevalence in HIV-infected PWID enrolled in an Antiretroviral Treatment Adherence Unit (AAU) over a period of 1 year, and to evaluate the reliability of cough as a screening symptom in TB diagnosis.

STUDY POPULATION AND METHODS

Study setting

The AAU is a residential rehabilitation facility for HIV-infected PWID offering combined treatment for opioid dependence with HIV treatment adherence support.[18] The AAU is located in Islamabad, Pakistan, and managed by the Nai Zindagi Trust (NZT), a local non-governmental organisation. This is the only centre of its type in Pakistan in which street-based, HIV-infected PWID are provided with treatment and care for 2 months. Only adult males (aged $\geqslant$18 years) deemed to be adequately motivated and fit to travel are referred to the AAU from different districts after providing written informed consent. Free travel by road is arranged for PWID in small groups. On admission, injectable drugs are withdrawn and their condition is managed symptomatically without substitute therapy. Antiretroviral treatment (ART) is initiated after withdrawal symptoms have been controlled.

In July 2015, a collaborative intervention by the Pakistan National Tuberculosis Control Programme (NTP) and NZT was implemented under routine programme conditions to systematically screen all PWID for active TB at enrolment to the AAU.

Study design and population

This was a cross-sectional study based on a retrospective record review among HIV-infected PWID enrolled in an AAU in Islamabad between August 2015 and July 2016.

The study protocol was approved by the National Bioethics Committee, Islamabad.

MATERIALS AND METHODS

In the first week of admission, all AAU inmates were briefed about TB and the associated elevated risk for the inmates during routine counselling sessions. All HIV-infected PWID regardless of symptoms were advised to submit sputum in the morning on a fixed day. Those who presented in the morning were given instructions on the collection of good-quality sputum. A standard laboratory referral form was used to record a short clinical history for those who submitted sputum. Samples collected were transported in a cool transport box on the same day to the National TB Reference Laboratory (NRL) in Islamabad.

Laboratory methods

The specimens were processed by the NRL, generally within 24 h of collection, using the *N*-acetyl-l-cysteine-sodium hydroxide (NaOH) method at a final concentration of 1.25% NaOH.[19] The sediment was used for smear, Xpert testing and culture on two slopes of Löwenstein-Jensen (LJ) medium, and one tube of MGIT™960™ (Mycobacterial Growth Indicator Tube; BD, Sparks, MD, USA). Auramine-stained smears were examined using light-emitting diode (LED) fluorescence microscopy. Positive culture isolates were identified for *Mycobacterium tuberculosis* using the TB Ag MPT64 RAPID® test (SD Bioline, Kyonggi, Korea). Phenotypic drug susceptibility testing was performed using MGIT960.

Data collection

Laboratory results and data on the specimen quality of the PWID were collected from the NRL electronic register. Data on demography, TB symptoms, including cough, fever and history of anti-tuberculosis treatment, contact with a known TB case, and smoking were collected using laboratory referral forms. Data on the total number of admissions to the AAU during the study period, district and province of origin, marital status and CD4 cell counts were collected from the electronic records of the AAU. All personal identifiers were removed from data files before analysis.

Statistical analysis

For the purposes of the study, all cases reported positive for *M. tuberculosis* on culture and/or Xpert were defined as 'bacteriologically confirmed TB'. Data were analysed using SPSS v18.0 (IBM, Armonk, NY, USA). Means, medians, standard deviations and interquartile ranges (IQRs) were calculated for continuous variables, and frequencies and percentages for categorical data. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to test the association between categorical variables.

RESULTS

From August 2015 to July 2016, a total of 888 HIV-infected PWID were enrolled at the AAU; the median age was 31 years (IQR 26–36) and median CD4 cell count was 423 cell/mm^3 (IQR 295–563). Of the 888 patients enrolled, 71.5% (n = 635) were screened, 90.4% of whom were smokers, 28.5% (n = 181) reported current cough, 8.5% (n = 54) complained of fever, 6.7% (n = 43) had cough with fever, 9.1% (n = 58) had a history of TB and 4.9% (n = 31) had had contact with a TB patient (Table 1). Seven were identified as already diagnosed TB cases on treatment.

Of 635 samples tested, respectively 10, 25 and 20

Table 1 Demographic characteristics of HIV-infected people who inject drugs admitted to the AAU, those screened for TB and bacteriologically confirmed TB cases, Pakistan, 2015–2016

	Admitted to AAU ($n = 888$) *n* (%)	Screened for TB ($n = 635$) *n* (%)	Bacteriologically confirmed TB ($n = 32$) *n* (%)
Age, years, median [IQR]	31 [26–36]	30 [26–36]	31 [26–36]
Age group, years			
<35	580 (65.3)	404 (63.6)	19 (59.4)
⩾35	295 (33.2)	218 (34.3)	11 (34.4)
Missing/not recorded	13 (1.5)	13 (2.0)	2 (6.3)
Origin			
Punjab Province	648 (73.0)	471 (74.2)	25 (78.1)
Sindh Province	240 (27.0)	164 (25.8)	7 (21.9)
Marital status			
Married	423 (47.6)	297 (46.8)	16 (50.0)
Unmarried/divorce/separated	419 (47.2)	292 (46.0)	11 (34.4)
Missing/not recorded	46 (5.2)	46 (7.2)	5 (15.6)
CD4 cell count, cell/mm^3			
<500	569 (64.1)	403 (63.5)	17 (53.1)
⩾500	273 (30.7)	186 (29.3)	10 (31.3)
Missing/not recorded	46 (5.2)	46 (7.2)	5 (15.6)
Current cough			
Yes	181 (20.4)	181 (28.5)	16 (50.0)
No	437 (49.2)	437 (68.8)	16 (50.0)
Missing/not recorded	270 (30.4)	17 (2.7)	0
Fever			
Yes	54 (6.1)	54 (8.5)	3 (9.4)
No	561 (63.2)	561 (88.3)	29 (90.6)
Missing/not recorded	273 (30.7)	20 (3.1)	0
Past history of TB			
Yes	58 (6.5)	58 (9.1)	2 (6.3)
No	555 (62.5)	555 (87.4)	30 (93.8)
Missing/not recorded	275 (31.0)	22 (3.5)	00 (0.0)
Home contact with TB patient			
Yes	31 (3.5)	31 (4.9)	2 (6.3)
No	578 (65.1)	578 (91.0)	30 (93.8)
Missing/not recorded	279 (31.4)	26 (4.1)	0
Smoking			
Yes	574 (64.6)	574 (90.4)	29 (90.6)
No	44 (5.0)	44 (6.9)	3 (9.4)
Missing/not recorded	270 (30.4)	17 (2.7)	0

HIV = human immunodeficiency virus; AAU = Antiretroviral Treatment Adherence Unit; TB = tuberculosis; IQR = interquartile range.

were reported positive for smear, Xpert and culture. Culture positivity was respectively 100% (2/2), 66.7% (4/6) and 41.2% (7/17) for specimens with medium, low and very low levels of *M. tuberculosis* detected on Xpert (Table 2). Among smear- and Xpert-negative samples, culture was positive in seven; *M. tuberculosis* was isolated in six of these using MGIT only. Xpert was positive for *M. tuberculosis* in 65% (13/20) of the culture-positive cases (Figures 1 and 2). In 10 cases reported as positive on Xpert only, culture failed to grow in 9 and NTM was overgrown in 1. Of these 10 TB cases, 8 had no history of previous anti-tuberculosis treatment, and 2 had undergone treatment more than a year before the current episode. Rifampicin (RMP) results were available in 29 cases; resistance was reported in 10% (3/29).

Taking into account 32 TB cases newly diagnosed and seven already on TB treatment, the prevalence of TB in HIV-infected PWID was estimated at 6141/100 000 (6.14%, 95%CI 4.4–8.3). Among newly diagnosed TB cases, 14 had symptoms of cough only, 2 had cough with fever, 1 had fever only and 15 had no cough or fever (Table 1). The proportion of smear-positives among TB cases was 37% (6/16) in those with cough compared to 18.8% (3/16) in those with no cough (Figure 1). A significantly higher prevalence of bacteriologically confirmed TB was reported in PWID with cough (8.8%; 95%CI 5.32–13.67) than in those with no cough (3.7%; 95%CI 2.18–5.75) and in smokers with a history of ⩾10 pack-years (6.94%; 95%CI 4.40–10.31) than in those with <10 pack-years (2.97%; 95%CI 1.20–6.01) (Table 3).

DISCUSSION

This retrospective study assessed TB prevalence among HIV-infected PWID referred to an AAU. Of

Table 2 Quantitative results of AFB smear, Xpert MTB/RIF assay and culture of HIV-infected PWID screened for TB in the AAU, Islamabad, Pakistan, 2015–2016

		Culture results				
AFB smear result	Xpert MTB/RIF assay result	*M. tuberculosis*-positive, MGIT/LJ result*	NTM-positive, MGIT/LJ result	Contaminated *n*	No growth *n*	Total *n*
Positive ($n = 3$)	*M. tuberculosis* detected: moderate	Positive/1+ ($n = 1$), positive/2+ ($n = 1$)	0	0	0	2
	M. tuberculosis not detected		Not applied/3+ ($n = 1$)	0	0	1
Scanty ($n = 7$)	*M. tuberculosis* detected: low	Positive/1+ ($n = 4$)	0	0	1	5
	M. tuberculosis detected: very low	Contaminated/1+ ($n = 1$)	0	1	0	2
Negative ($n = 625$)	*M. tuberculosis* detected: low				1	1
	M. tuberculosis detected: very low	Positive/1 colony ($n = 1$), positive/1+ ($n = 1$), positive/6 colonies ($n = 1$), positive/contaminated ($n = 2$), contaminated/1+ ($n = 1$)	Positive/no growth ($n = 1$)	0	8	15
	M. tuberculosis not detected	Positive/no growth ($n = 6$), not applied/1+ ($n = 1$)	Positive/contaminated ($n = 1$), positive/no growth ($n = 2$)	28	559	597
	Invalid/error	0	0	1	11	12
Total, *n* (%)		20 (3.1)	5 (0.8)	30 (4.7)	580 (91.3)	635

* 1+ = 10–100 colonies on LJ medium; 2+ = >100–200 colonies on LJ medium; 3+ = >200 colonies on LJ medium
AFB = acid-fast bacilli; HIV = human immunodeficiency virus; PWID = people who inject drugs; TB = tuberculosis; AAU = Antiretroviral Treatment Adherence Unit; MGIT = Mycobacterial Growth Indicator Tube; LJ = Löwenstein-Jensen; NTM = non-tuberculous mycobacteria.

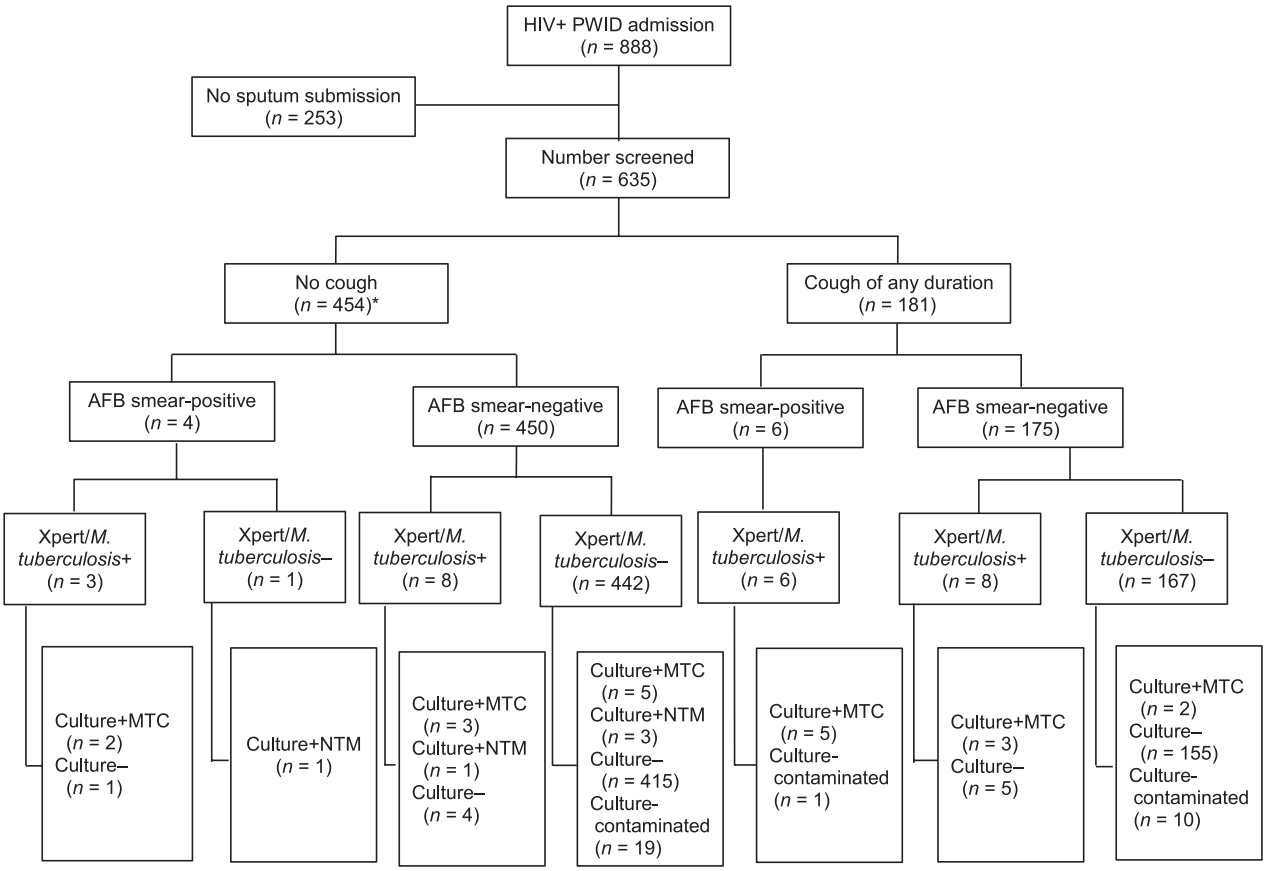

Figure 1 Flow diagram showing laboratory results of HIV+ PWID screened for tuberculosis in the AAU, Islamabad, Pakistan, 2015–2016. *Includes 17 cases with information not recorded on cough symptoms. HIV = human immunodeficiency virus; + = positive; PWID = people who inject drugs; AFB = acid-fast bacilli; – = negative; MTC = *M. tuberculosis* complex; NTM = non-tuberculous mycobacteria.

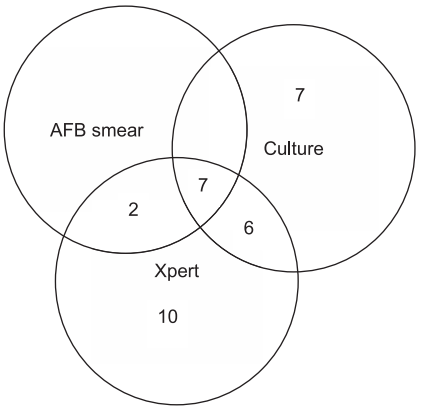

Figure 2 Diagnostic profile of 32 bacteriologically confirmed TB cases detected on active screening of HIV-positive people who inject drugs admitted to the AAU, Islamabad, Pakistan, 2015–2016. AFB = acid-fast bacilli; TB = tuberculosis; HIV = human immunodeficiency virus; AAU = Antiretroviral Treatment Adherence Unit.

888 subjects, 71.5% submitted a sputum sample for testing regardless of symptoms; no chest X-rays were performed but all patients were asked about cough and fever (TB symptoms), TB contact history, TB treatment history and smoking. All specimens were tested using AFB smear, Xpert and culture, and 32 new TB cases were detected. RMP resistance was reported in 10% (3/29) of newly identified TB cases.

To our knowledge, this is the first study from Pakistan on systematic screening for active TB in HIV-infected injectable drug users. The estimated TB prevalence of 6141/100 000 in this key population is 15-fold higher than in the general adult population (398/100 000).[2] Limitations that may have contributed to an underestimation of TB prevalence were the exclusion of PWID who reported sick, those who lacked motivation to seek treatment and those reported smear-positive on pre-referral screening. Furthermore, the use of a single specimen for diagnosis may have contributed to underestimation. As information was available for cough and fever only, the WHO-recommended four symptom-based screening approach could not be fully evaluated for this key population.[13,20,21]

According to the 2015 World Drug Report, there are an estimated 12.7 million PWID worldwide, 13.5% of whom are HIV-infected.[22] Two prospective studies, one in Amsterdam, the Netherlands, and other in New York, NY, USA, both showed an elevated risk of TB activation in HIV-positive drug users.[23,24] In a study conducted in Tanzania, the WHO-recommended[13,21] symptom screening process was used for active case finding in 150 PWID on a

Table 3 Univariate regression analysis of the factors associated with bacteriologically confirmed TB in HIV-positive PWID screened for TB in the AAU, Islamabad, Pakistan, 2015–2016

	Tested *n*	TB cases *n* (%)	OR (95%CI)	*P* value
Origin (Province)				
Punjab	471	25 (5.3)	Reference	
Sindh	164	7 (4.2)	0.79 (0.33–1.87)	0.601
Marital status				
Married	297	16 (5.39)	Reference	
Unmarried	292	11 (3.77)	0.68 (0.31–1.50)	0.350
CD4 cell count, cells/mm^3				
⩾500	186	10 (5.38)	Reference	
<500	403	17 (4.22)	0.78 (0.34–1.74)	0.533
Unknown	46	5 (10.87)	2.14 (0.69–6.61)	1.840
Cough				
No	437	16 (3.66)	Reference	
Yes	181	16 (8.84)	2.55 (1.24–5.20)	0.010
Cough duration, weeks				
<2	105	8 (7.62)	Reference	
>2	69	8 (11.59)	1.59 (0.50–4.45)	0.378
Smoking, pack-years				
<10	236	7 (2.97)	Reference	
⩾10	317	22 (6.94)	2.43 (1.02–5.81)	0.040
History of anti-tuberculosis treatment				
No	555	30 (5.4)	Reference	
Yes	58	2 (3.4)	0.62 (0.15–2.68)	0.527
Quality of sample				
Purulent, mucoid	301	19 (6.3)	Reference	
Saliva	334	13 (3.9)	0.60 (0.29–1.23)	0.168
Quantity of sample, ml				
>2	430	24 (5.5)	Reference	
⩽2	205	8 (3.9)	0.68 (0.30–1.55)	0.368

TB = tuberculosis; HIV = human immunodeficiency virus; PWID = people who inject drugs; AAU = Antiretroviral Treatment Adherence Unit; OR = odds ratio; CI = confidence interval.

methadone maintenance programme. Two samples from symptomatic individuals were examined using smear and culture, and active TB was reported in 4% of PWID, which was 23 times the national TB prevalence.[25] In a study by Adelman et al., symptom screening was used in combination with Xpert testing in PLHIV and 6% were detected as having active TB.[26] In our study, a single morning specimen was examined, regardless of symptoms. PWID with cough showed a significantly higher odds of testing positive for TB (OR 2.55, 95%CI 1.24–5.20); however, an equal number of TB cases was also diagnosed among PWID with no cough. We reported a 22- and 9-fold higher prevalence of TB in PWID with cough and those without cough, respectively, compared with the general adult population. These findings are in agreement with evidence from recent prevalence surveys[2,27] showing the inadequate performance of symptom screening alone in detecting TB. However, the possible role of opiates in suppressing cough, and further lowering of the diagnostic value of cough in TB screening in this key population cannot be excluded.[9,12]

In a study conducted in Malaysia, a single specimen from 125 HIV-infected prisoners was examined using Xpert and liquid culture. A TB prevalence of 16.7% and Xpert sensitivity of 53% were reported.[28] In our study, Xpert was positive in 65% (13/20) of culture-confirmed TB cases; however, 12 Xpert-positive cases were not confirmed on culture. The detection of dead bacilli on Xpert in culture-negative cases can be ruled out, as none of these PWID had a recent history of anti-tuberculosis treatment. However, as X-rays were not performed, there remained a potential risk of false-positive results, especially among those with a lower pre-probability of TB, such as those with no cough. In a systematic review on Xpert testing in adults by Steingart et al. at an overall estimated prevalence of 5% in PLHIV and using a pooled sensitivity of 78% and specificity of 98%, the positive predictive value was estimated at 72%.[29] In our study, five of the 10 TB cases positive only on Xpert had no cough. Nevertheless, culture itself also has limitations, and factors such as delays in processing paucibacillary specimens, suboptimal quality and quantity of specimens, testing priority given to Xpert testing and the growth of non-tuberculous mycobacteria and other contaminating bacteria in culture media may have contributed to false-negative results. Use of a higher final concentration of NaOH (1.25% vs. 1.0%) to process specimens with a very low number of bacilli may have resulted in the failure of culture to grow, as has also been reported in a comparative study by Pares et al.[30]

In Pakistan, there are an estimated 105 000 injectable drug users, 27% of whom are HIV-infected;[3,4] currently only 2316 are on ART.[31] Based on a TB prevalence of 6.1%, estimated TB cases in this key population would account for <1% of Pakistan's total disease burden. However, keeping in mind the disproportionately high TB prevalence in this key population, a systematic, targeted approach to TB case finding and care is required. Systematic screening services for PWID referred to AAU have been maintained, but the scale-up of services offering intensified TB case finding and wider access to new diagnostic tools are needed for PWID across Pakistan. Cough has been shown to have a low diagnostic value in detecting TB among HIV-infected PWID, as half of the TB cases and one third of smear-positive infective TB cases had no cough. Further studies are needed to evaluate the case-finding strategies best suited for this most vulnerable and marginalised group of the population.

In conclusion, we found TB prevalence in HIV-infected PWID (6.1%) to be 15 times higher than in the general adult population. Cough has a low diagnostic value in detecting TB. Xpert testing led to the detection of greater number of TB cases than smear and/or culture.

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Conflicts of interest: none declared.

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RÉSUMÉ

CONTEXTE : Le Pakistan est un pays lourdement frappé par la tuberculose (TB), passant d'une faible prévalence du virus de l'immunodéficience humaine (VIH) à une épidémie concentrée, principalement alimentée par les utilisateurs de drogues injectables (PWID). L'unité d'adhérence au traitement antirétroviral (AAU) est une structure résidentielle qui offre un traitement combiné de la dépendance aux opioïdes et du VIH.

OBJECTIF ET SCHÉMA : Cette étude rétrospective a été réalisée afin d'évaluer la prévalence de la TB parmi les personnes infectées par le VIH, référées à l'AAU et d'évaluer la valeur diagnostique de la toux comme outil de dépistage. Un seul échantillon de crachats a été recueilli, sans tenir compte des symptômes, et a été examiné par frottis, Xpert® MTB/RIF et culture.

RÉSULTATS : Des 888 PWID, 71,5% ont soumis un échantillon de crachats. L'Xpert a détecté plus de cas de TB ($n = 25$) que le frottis ($n = 10$) et la culture ($n = 20$). La prévalence de la TB a été estimée à 6141/100 000 en tenant compte des sept cas identifiés déjà sous traitement de TB et des 32 cas de TB nouvellement diagnostiqués et confirmés par bactériologie. A la fois la toux et le fait de fumer ($\geqslant 10$ paquets-années) ont été associés avec une prévalence élevée de TB. Seulement la moitié des cas de TB ont rapporté une toux. La résistance à la rifampicine a été rapportée chez 10% (3/29) des cas nouvellement identifiés.

CONCLUSION : La prévalence de la TB parmi les personnes infectées par le VIH est 15 fois plus élevée que dans la population générale adulte. La toux a une faible valeur diagnostique en tant que symptôme de dépistage.

RESUMEN

MARCO DE REFERENCIA: El Pakistán es un país con una alta carga de morbilidad por tuberculosis (TB), que evoluciona de una baja prevalencia de infección por el virus de la inmunodeficiencia humana (VIH) hacia una epidemia concentrada, determinada sobre todo por las personas que se inyectan drogas (PWID). La iniciativa de la unidad de adhesión al tratamiento antirretrovírico (AAU) consiste en un establecimiento residencial que ofrece tratamiento conjunto a la dependencia a los opioides y a la infección por el VIH.

OBJETIVO Y MÉTODO: El presente estudio retrospectivo se llevó a cabo con el fin de determinar la prevalencia de TB en las PWID aquejadas de infección por el VIH, y remitidas a la AAU y evaluar el valor diagnóstico de la tos como un síntoma de detección sistemática. Se recogió una sola muestra de esputo, con independencia de los síntomas, y se examinó mediante la baciloscopia, la prueba Xpert® MTB/RIF y el cultivo.

RESULTADOS: De las 888 PWID inscritas en la AAU, el 71,5% aportó una muestra de esputo. La prueba Xpert detectó más casos de TB ($n = 25$) que la baciloscopia ($n = 10$) y el cultivo ($n = 20$). Se estimó una prevalencia de TB de 6141/100 000 habitantes, incluidos siete casos detectados que ya recibían tratamiento antituberculoso y 32 casos nuevos diagnosticados y confirmados bacteriológicamente. Dos síntomas, la tos y el tabaquismo ($\geqslant 10$ paquetes-año), se asociaron con una alta prevalencia de TB. Solo la mitad de los casos de TB refirió tos. Se notificó resistencia a rifampicina en el 10% (3 de 29) de los casos nuevos diagnosticados.

CONCLUSIÓN: La prevalencia de TB en las PWID que padecen infección por el VIH es 15 veces superior a la prevalencia en la población general. La tos como síntoma de detección sistemática ofrece un bajo valor diagnóstico.