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TB Diagnostic Capacity in Sub-Saharan African HIV Care Settings

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Abstract

As HIV care services continue to scale-up in sub-Saharan Africa, adequate tuberculosis diagnostic capacity is vital to reduce mortality among HIV-infected persons. A structured survey was administered at 663 health facilities providing HIV care to 908,043 patients in across 9 sub-Saharan African countries to estimate the proportion of facilities and HIV patients at these facilities with access TB-related diagnostic tests. Sputum smear microscopy was available at 87% of facilities (representing 97% of patients), chest x-ray at 26% of facilities (representing 56% of patients), tuberculin skin tests were available at 12% of facilities (representing 33% of patients). Acid-fast bacillus culture was available on-/off-site at 53% of facilities (representing 77% of patients). Primary health facilities had lower availability of tuberculosis diagnostic tests compared with secondary and tertiary health facilities. As HIV care continues to decentralize to primary health facilities, a corresponding expansion of diagnostic capacity to lower levels of the health system will be essential.

Keywords

tuberculosis diagnostics; laboratory capacity; TB/HIV integration; HIV care; implementation science; resource-limited settings

INTRODUCTION

Fueled by the HIV epidemic, tuberculosis (TB) remains a global public health challenge. In 2010, there were 8.8 million incident cases of TB worldwide and 1.45 million deaths.[1] An estimated 1.1 million incident cases were HIV-coinfected; 82% of these were in sub-Saharan Africa (SSA), where drug-resistant TB is also an emerging threat.[1]

Intensified TB case finding and prompt initiation of TB treatment are important strategies to improve patient outcomes and curb transmission, particularly among HIV-infected patients,

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who often present with atypical disease. However, lack of adequate diagnostic capabilities in resource-limited settings where HIV-infected persons receive care often delays diagnosis. In turn, initiation of treatment for active TB and isoniazid preventive therapy (IPT) for those in whom active TB was excluded is often delayed.[1] According to the most recent WHO estimates, in SSA, smear microscopy coverage is at 1.4 laboratories per 100,000 population, acid-fast bacilli (AFB) culture coverage at 0.7 laboratories per 5 million population, and drug susceptibility testing (DST) coverage at 0.4 laboratories per 10 million population. By contrast, in resource-rich countries such as Germany, coverage of AFB culture and DST is at 12 laboratories per 5 million population and 4.4 laboratories per 10 million population, respectively.[1] Improving the coverage and capacity of laboratories with adequate TB diagnostic services is a global health priority, especially in SSA where HIV prevalence is high and the incidence of multidrug and extensively drug-resistant TB (MDR/XDR-TB) is increasing.[2] We describe the availability of TB diagnostic services at 663 diverse health facilities across 9 SSA countries.

METHODS

In September 2010, a structured survey was administered to staff in 663 health facilities supported by ICAP-Columbia University providing HIV care and treatment across 9 SSA countries funded by the President's Emergency Plan for AIDS Relief (Cote d'Ivoire, Ethiopia, Kenya, Mozambique, Nigeria, Rwanda, South Africa, Swaziland, and Tanzania). These facilities represented 97% of all HIV care and treatment facilities that received support from ICAP at the time. The survey consisted of 101 questions about the HIV program and facility characteristics, of which 23 questions were TB-related. The survey was administered by ICAP field staff to the director of the health facility, HIV clinic, or another staff member most familiar with the day-to-day operations of the facility. The protocol was reviewed by Columbia University Institutional Review Board and received nonhuman subject research determination, as the subjects of data collection were facilities and not individuals.

Outcome variables for the present analysis included availability of sputum smear microscopy, chest x-ray (CXR), and tuberculin skin test (TST) on-site and availability of AFB culture and DST on-site or through referral to another facility (data cannot be disaggregated). Covariates in the present analysis were facility characteristics, including location (urban and rural), facility type (public primary, public secondary, public tertiary, and private/other), and time since first quarter of reporting as a proxy for years providing comprehensive HIV care. In addition, patient load at the HIV clinic was derived from cumulative enrollment data reported during the July–September 2010. We examined the frequencies of available TB diagnostic tests stratified by facility characteristics. Furthermore, we estimated the proportion of HIV-infected patients enrolled in care at facilities that might have access to these tests, disregarding operational barriers, such as provider knowledge, fees for tests, and equipment malfunction, by dividing the number of patients enrolled in facilities reporting availability of various TB diagnostic tests by the total number of patients enrolled. Statistical significance was assessed with χ^2 tests, with $P < 0.05$ as threshold for significance. Statistical analyses were performed using SAS software version 9.2 (SAS, Cary, NC).

RESULTS

As of September 2010, 908,043 HIV-infected patients were cumulatively enrolled in HIV care at the 663 facilities included in this analysis (Table 1). The majority (59%) of facilities surveyed was public sector primary care facilities and was evenly distributed between urban and rural areas. However, in terms of number of patients, most patients were enrolled at

public sector secondary and tertiary facilities (63%) and in urban facilities (78%). The median cumulative number of patients ever enrolled across the surveyed facilities was 365 (IQR: 96–1419), with children aged 0–14 comprising 9.3% of the patients. The median time since a facility began providing comprehensive HIV care was 2.0 years (IQR: 0.75–3.5). Most facilities reported offering TB treatment within the facility (80%).

Sputum smear microscopy, CXR, and TST were reported available on-site at 87% [range across country programs (RAC): 28%–100%], 26% (RAC: 8%–79%), and 12% (RAC: 0%–60%) of facilities, respectively. Fifty-three percent (RAC: 2%–94%) of facilities had AFB culture availability either on-site or through another facility, and of these facilities, 35% (RAC: 0%–75%) had availability of DST on-site or through another facility.

Table 2 compares on-site availability of each diagnostic test by facility characteristics. While sputum smear microscopy was widely available across urban and rural areas at all types of facilities (public primary, public secondary, public tertiary, and private/other), CXR availability varied substantially from 0% to 94%, and TST availability was low across facilities (Table 2). Availability of CXR was high in urban secondary and tertiary facilities (74% and 94%, respectively) and lower in urban private and rural secondary facilities (55% and 48%, respectively). CXR was rarely available in urban and rural primary facilities (both at 3%). TST availability was highest at urban tertiary facilities (44%), while all other facilities reported very low availability.

Availability of AFB culture on-site or through referral to another facility was also variable and was highest at urban tertiary (81%) and rural secondary (77%) facilities. Among 352 facilities with AFB culture availability, DST was most available in urban tertiary facilities (69%), followed by private (56%) and public primary facilities (41%). Facilities providing HIV care for ≥5 years or having ≥352 cumulative patients in HIV care were more likely to have all specified types of diagnostic tests available (with the exception of DST), as compared with facilities that more recently initiated HIV care programs and/or had fewer patients enrolled in care. Facilities providing HIV care for ≥5 years were less likely to have availability of DST compared with facilities providing HIV care for <1 year (26% vs 50%).

When examining the proportion of HIV-infected patients at facilities that reported having availability of TB diagnostic tests, disregarding operational barriers, a higher proportion of patients as compared with facilities had availability of diagnostic tests. This is mainly because, as stated above, most HIV-infected patients accessing care in surveyed facilities do so at secondary and tertiary facilities where there is relatively high availability of TB diagnostics tests. Of all HIV-infected patients receiving care at surveyed facilities, 97%, 56%, and 33% of patients attended facilities that had on-site sputum smear microscopy, CXR, and TST, respectively. Seventy-seven percent and 35% of patients attended facilities that had AFB culture availability and DST either on-site or through another facility, respectively.

DISCUSSION

In this survey of the availability of TB diagnostic tests at 663 HIV care and treatment facilities from 9 SSA countries, we found that sputum smear microscopy was widely available across the spectrum of healthcare facilities, irrespective of location and type of facility. However, availability of CXR, TST, and AFB culture were generally limited to secondary and tertiary facilities. Surprisingly, DST was more commonly available at primary as opposed to secondary facilities, and at those providing HIV care for <1 as opposed to ≥5 years, findings partly driven by the large number of primary and less mature facilities included in the survey from Kenya and South Africa, respectively, where DST was

reportedly available at all health facility levels. Still, with exception of South Africa, none of the countries included in the analysis have achieved the Global Plan to Stop TB goal for countries with high prevalence of HIV (and consequently smear-negative TB) of at least one laboratory with AFB culture and DST capability per 5 million population.[4] TST was only available at a small number of facilities. The lack of CXR and TST availability demonstrates the difficulty in operationalizing TB diagnostic algorithms developed in many countries for HIV-infected patients that include CXR, and in the case of children TST,[5] given the high prevalence of paucibacillary disease[6] and the challenges inherent to diagnosing TB in such patients.[7] The lack of availability of TST capacity also demonstrates the difficulty in attempting to identify HIV-infected patients most likely to benefit from IPT, that is, those with positive TST.[8]

In our analysis, only 53% of facilities reported on-site or off-site availability of AFB culture, most likely because in many resource-limited settings, particularly with high TB incidence, AFB culture is not included in national diagnostic algorithms for patients without a history of TB because of its cost and a turnaround time that can span 6–8 weeks.[9] Nevertheless, because most patients were enrolled in secondary and tertiary facilities, culture availability in terms of the number of HIV-infected patients was relatively high, at 77%. Similarly, only 12% and 26% of facilities reported having on-site availability of TST and CXR, respectively. However 33% and 56% of HIV-infected patients attended facilities that reported having these diagnostic tests. These proportions may decrease in the near future, as HIV care becomes further decentralized and increasing numbers of patients receive HIV care in primary care settings where availability of such tests is more limited. As HIV care expands to primary health facilities across SSA, it is anticipated that TB incidence will decline because of increased ART coverage.[2] Nonetheless, continued scale-up of laboratory and CXR service availability to lower levels of the health care system is critical to prevent delays in TB diagnosis and treatment, particularly in the context of the rapid increase in incidence of MDR/XDR-TB noted in recent years.[3]

The study had some limitations worth noting. The data were based on responses of health facility staff and were not always independently verified by survey staff. As such, we cannot rule out the possibility of facility staff over- or underreporting availability of diagnostic tests. In addition, the facility survey only determined the availability of diagnostic tests and did not assess patient access and routine use of these tests, which may have been limited by factors such as provider awareness, equipment malfunction, and direct and indirect costs to patients. For example, the finding that AFB culture is available at 53% of clinics may not always reflect routine use of this test for TB diagnostic purposes and should be interpreted with caution. In many cases, clinics must transport specimens to central laboratories in the capital cities for AFB culture testing. Routine utilization of the test and access to test results in a timely fashion are likely present at less than 53% of facilities (and subsequently less than 77% of HIV patients).

Strengths of this study include the breadth of the HIV care facilities surveyed, which included predominantly public facilities at all levels of the health care system in both urban and rural areas in 9 SSA countries with high TB case rates.[1] Furthermore, the survey was found to have good test–retest reliability; a data quality assurance exercise performed in 2010 that recollected data on a sample of questions (including 3 TB screening and diagnostic test questions) from the 2009 facility survey found 81% (IQR: 74%–85%) agreement.[10]

In conclusion, as HIV care expands to primary health facilities across SSA, a corresponding expansion of TB-related laboratory and radiology services to lower levels of the health care system is essential to meet the expected increase in demand for such services. Without it,

availability of timely TB diagnosis and treatment for HIV-infected individuals may decrease in the coming years. These efforts should include increasing availability of CXR and TST to implement comprehensive TB diagnostic algorithms and ensure timely initiation of treatment for active TB and uptake of IPT for latent TB infection. Given the increasing threat of MDR/XDR-TB in the region,[3] increasing availability of AFB culture and DST through strengthened linkages between lower and higher level facilities is critical, including improvements in specimen transportation systems. Given the various performance and implementation issues with existing tests, especially in settings with high TB/HIV coinfection,[6] expanding coverage of rapid molecular tests, such as Xpert MTB-RIF (Xpert; Cepheid, Inc, Sunnyvale, CA), is also a potentially important strategy.[11–13] However, scale-up of molecular tests will face challenges similar to those of AFB culture because of their relatively high cost and prerequisite environmental conditions, such stable electrical supply and adequate room temperature, which are difficult to achieve in primary health care facilities in resource-limited settings.[13,14] Existing diagnostic tests can improve timely diagnosis and treatment of TB among HIV-infected patients. Resources are needed to expand the coverage of these tests to lower level health facilities where a substantial number of patients are expected to receive HIV care and treatment in the near future.

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TABLE 1

Clinic Characteristics at 663 HIV Care and Treatment Programs in 9 SSA Countries, September 2010

	Total Facilities, n (%)	Total Patients, n (%)
HIV Care and Treatment Clinics	663	908,043
Country		
Cote d'Ivoire	60 (9)	9868 (1)
Ethiopia	62 (9)	96,762 (11)
Kenya	157 (24)	137,002 (15)
Mozambique	60 (9)	278,083 (31)
Nigeria	33 (5)	83,382 (9)
Rwanda	46 (7)	46,139 (5)
South Africa	69 (10)	121,835 (13)
Swaziland	49 (7)	67,697 (7)
Tanzania	127 (19)	67,275 (7)
Location and clinic type		
Urban		
Public primary*	157 (24)	184,119 (20)
Public secondary†	129 (19)	400,792 (44)
Public tertiary‡	16 (2)	101,012 (11)
Private/other§	32 (5)	31,571 (3)
Rural		
Public primary	229 (35)	100,708 (11)
Public secondary	53 (8)	75,308 (8)
Private/other	47 (7)	14,533 (2)
Cumulative in number of patients in HIV care (proxy for program size)‖		
<365	328 (50)	41,288 (5)
≥365	328 (50)	866,755 (95)
Missing	7	
Years providing comprehensive HIV care (proxy for program maturity)		
≥5 yrs	51 (8)	251,906 (28)
ge;3 and <5 yrs	160 (24)	375,389 (41)
≥1 and <3 yrs	362 (55)	260,000 (29)
<1 yr	90 (14)	20,748 (2)
Provide treatment of active TB within the facility		
Total	530 (80)	793,700 (87)

*Health centers and clinics.

†District/provincial hospitals.

‡Teaching/national referral hospitals.

§Private: any facility run by private, nongovernmental, or faith-based organization; Other: mixed private–public clinics, workplace clinics, VIP clinic, and other clinic types.

[||]Cumulative through September 30, 2010. The categories were created using the median.

TABLE 2

Bivariate Analysis of Factors Associated With Availability of Sputum Smear, Sputum Culture, DST, CXR, and TST Diagnostic Services at HIV Care and Treatment Programs in 9 SSA Countries, September 2010 (N = 663)*

	Sputum Smear Microscopy (n = 660)		AFB (n = 663)		DST (n = 352)†		CXR (n = 653)		TST (n = 663)	
	n (%)	*P*	n (%)	*P*	n (%)	*P*	n (%)	*P*	n (%)	*P*
Overall (% facilities)	574 (87)		352 (53)		123 (35)		170 (26)		81 (12)	
Overall (% patients)	881,972 (97)		699,968 (77)		242,640 (35)		508,757 (56)		301,117 (33)	
Location and clinic type										
Urban										
Public primary	**118 (76)**	**0.0039**	**71 (45)**	**0.0106**	27 (38)	0.7075	4 (3)	0.7813	**41 (26)**	**<0.0001**
Public secondary	**127 (99)**	**<0.0001**	72 (56)	0.568	**17 (24)**	**0.0208**	**93 (74)**	**<0.0001**	**17 (13)**	**0.0003**
Public tertiary	15 (94)	0.3768	**13 (81)**	**0.0152**	**9 (69)**	**0.0124**	**15 (94)**	**<0.0001**	**7 (44)**	**<0.0001**
Private/other	27 (84)	0.5776	**9 (28)**	**0.0102**	5 (56)	0.3259	**17 (55)**	**<0.0001**	**3 (9)**	**0.0389**
Rural										
Public primary	202 (88)	Ref	135 (59)	Ref	55 (41)	Ref	7 (3)	Ref	5 (2)	Ref
Public secondary	**52 (98)**	**0.0005**	**41 (77)**	**0.0033**	**7 (17)**	**0.0156**	**25 (48)**	**<0.0001**	**8 (15)**	**0.0004**
Private/other	**33 (70)**	**0.0199**	**11 (23)**	**0.0006**	3 (27)	0.4251	**9 (19)**	**0.0001**	0 (0)	—
Cumulative number of patients in HIV care										
<365	250 (77)	Ref	124 (38)	Ref	45 (36)	Ref	30 (9)	Ref	14 (4)	Ref
≥365	**319 (98)**	**<0.0001**	**227 (69)**	**<0.0001**	78 (34)	0.716	**139 (43)**	**<0.0001**	**67 (20)**	**<0.0001**
Years providing comprehensive HIV care										
≥5 years	**50 (98)**	**0.000**	**39 (76)**	**<0.0001**	**10 (26)**	**0.037**	**43 (84)**	**<0.0001**	**15 (29)**	**0.005**
≥3 and <5 years	159 (100)	—	**110 (69)**	**0.000**	44 (40)	0.273	**74 (48)**	**<0.0001**	28 (18)	0.120
≥1 and <3 years	**302 (84)**	**0.046**	167 (46)	0.312	**51 (31)**	**0.015**	42 (12)	0.870	29 (8)	0.541
<1 year	63 (71)	Ref	36 (40)	Ref	18 (50)	Ref	11 (12)	Ref	9 (10)	Ref
Country										
Cote d'Ivoire	17 (28)	—	**1 (2)**	**0.000**	0 (0)	—	5 (8)	**0.014**	1 (2)	0.082
Ethiopia	62 (100)	1.000	37 (60)	0.406	1 (3)	0.152	49 (79)	**<0.001**	1 (2)	0.077
Kenya	147 (94)	0.639	**135 (86)**	**0.023**	41 (30)	0.077	21 (13)	**0.021**	0 (0)	0.999
Mozambique	57 (95)	0.714	**52 (87)**	**0.028**	**19 (37)**	**0.038**	17 (28)	0.962	**36 (60)**	**<0.001**
Nigeria	32 (100)	1.000	**10 (30)**	**0.005**	2 (20)	0.577	14 (48)	0.079	6 (18)	0.079

	Sputum Smear Microscopy (n = 660)		AFB (n = 663)		DST (n = 352)†		CXR (n = 653)		TST (n = 663)	
	n (%)	*P*	n (%)	*P*	n (%)	*P*	n (%)	*P*	n (%)	*P*
Rwanda	45 (100)	Ref	31 (67)	Ref	4 (13)	Ref	12 (28)	Ref	5 (11)	Ref
South Africa	67 (99)	0.889	**65 (94)**	**0.002**	**49 (75)**	**0.000**	15 (22)	0.510	**28 (41)**	**0.003**
Swaziland	37 (76)	0.118	**10 (20)**	<**0.0001**	1 (10)	0.810	9 (18)	0.281	0 (0)	—
Tanzania	110 (87)	0.350	**11 (9)**	<**0.0001**	**6 (55)**	**0.008**	28 (22)	0.442	4 (3)	0.056

*The table excludes missing values.

†Only answered by facilities with sputum culture diagnostic services.

Bold values indicate significance at $P < 0.05$.