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# Assessing capacity for diagnosing tuberculosis in children in sub-Saharan African HIV care settings

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## Summary

Research on the prevalence of pediatric-specific tuberculosis (TB) diagnostics in sub-Saharan Africa is scarce. We assessed the availability of pediatric TB diagnostic tests at 651 pediatric human immunodeficiency virus care and treatment sites across nine African countries: 54% of the sites had access to sputum culture capacity and 51% to chest X-ray services. While 87% of sites had access to smear microscopy, only 6% had the capacity to perform sputum induction and 5% to perform gastric aspirate. These findings confirm that diagnostic resources for the accurate diagnosis of pediatric TB are limited. Capacity-building initiatives to improve sputum collection in children are urgently required.

### Keywords

tuberculosis; HIV; pediatric; diagnosis

THE DIAGNOSIS of tuberculosis (TB) in children living with the human immunodeficiency virus (HIV) in sub-Saharan Africa is challenging:[1] sputum and culture confirmation rarely exceeds 30–40%.[2] In most instances, the diagnosis of TB is based on clinical criteria alone.[3] The clinical difficulties of diagnosing TB in HIV-positive children are well described. However, accurate diagnosis is also limited by programmatic limitations: specifically, the limited capability to acquire sputum samples in children unable to expectorate and the lack of trained personnel to perform and interpret TB diagnostic procedures in children.

In the present analysis, we describe the availability of TB diagnostic procedures and tests at sites providing pediatric HIV services in nine sub-Saharan countries. We sought to determine the proportion of sites that had access to chest X-ray (CXR), sputum culture and smear microscopy, and how many reported a capacity to perform sputum induction, naso-pharyngeal aspirate (NPA) and gastric aspirate (GA). We also sought to determine facility characteristics associated with the presence of these diagnostic capabilities.

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## Methods

In September 2010, we surveyed 651 sites providing HIV services in nine countries (Cote d'Ivoire, Ethiopia, Kenya, Mozambique, Nigeria, Rwanda, South Africa, Swaziland and Tanzania) that received support from the International Center for AIDS Care and Treatment Programs (ICAP) at Columbia University, New York, through funding from the government of the United States. National policy in each of these countries includes routine screening for TB in HIV-infected children.

Survey questions included access to TB diagnostic tests (smear microscopy, CXR and sputum culture onsite or offsite), capacity to perform specific pediatric TB diagnostic procedures (sputum induction, GA and NPA) and program characteristics. All sites provided HIV services to HIV-infected and HIV-exposed children aged 0–15 years. A recent assessment of this annual survey showed 83% test-retest agreement across multiple countries.[4] $\chi^2$ tests were used to assess the association of program and facility characteristics with the capacity to perform or with access to the following pediatric TB diagnostic procedures or tests: smear microscopy, GA, sputum induction, NPA, sputum culture and CXR. We examined the presence of these procedures or tests in relation to location (urban, semi-urban, rural, defined as per Demographic and Health Surveys criteria[5]), facility type (primary, secondary, tertiary and private), program maturity (years since initiation of pediatric HIV services), and overall program size (cumulative number of children and adults enrolled in care). Statistical analysis was performed using SAS software version 9.2 (SAS, Cary, NC, USA).

The protocol was reviewed by the Institutional Review Board of the Columbia University, New York, and received non-human subject research determination.

## Results

As of September 2010, 651 sites surveyed in this analysis had cumulatively enrolled 82 413 HIV-infected and HIV-exposed children (Table 1). Sputum smear microscopy was available at 87% of the sites, serving 98% of all children enrolled in care ($n$ = 565 sites, range across countries [RAC] 28–100%); 5% ($n$ = 34, RAC 0–21%) had the capacity to perform GA collection, 6% ($n$ = 39, RAC 0–24%) had the capacity to perform sputum induction and 2% ($n$ = 12, RAC 0–7%) had the capacity to perform NPA. Mycobacterial culture (performed onsite or offsite) was available at 54% ($n$ = 352, RAC 2–97%) of the sites. Nearly all sites with advanced capacity to obtain sputum (sputum induction and GA) performed sputum culture; however, respectively only 10% and 8% of the sites with access to sputum culture had sputum induction or GA capacity; 51% ($n$ = 330, RAC 18–89%) had access to CXR, performed either onsite or offsite.

In bivariate analysis, availability of TB diagnostics (Table 2) and the capacity to procure sputum samples (Table 3) were more likely at urban than rural sites, with the exception of sputum induction. Tertiary and secondary sites were more likely to have the capacity to perform GA (4% vs. 10%, $P$ = 0.0037) and sputum induction (3% vs. 13%, $P$ < 0.001) and

have access to CXR (36% vs. 84%, $P < 0.001$) compared to primary care sites. CXR (33% vs. 69%, $P < 0.001$) was more prevalent at sites with larger HIV programs.

## Discussion

The findings of our analysis are cause for alarm, given the high toll of disease and death among HIV-infected children in Africa. While the majority of the sites had the capacity to perform smear microscopy and had access to mycobacterial culture, essential for diagnosing TB in *both* adults and children, a much smaller fraction had capacity to perform any of the sputum collection procedures necessary in children unable to expectorate.

Given the limitations of clinical criteria alone in diagnosing TB in children with HIV,[6,7] it is worrying that relatively few sites have the capacity to obtain pediatric sputum samples for microscopy and culture. Lack of resources was particularly acute at primary care sites and at sites located in rural areas. These findings highlight the urgent need to increase access to accurate TB diagnostics in areas of high HIV prevalence and TB endemicity. To be effective, scale-up in access needs to occur commensurate with the policy of decentralizing HIV services from tertiary/secondary to primary care sites that is ongoing in many sub-Saharan countries.

There are several exciting developments in the field of TB diagnostics, including Cepheid's GeneXpert system, Xpert® MTB/RIF (Sunnyvale, CA, USA).[8] However, the accuracy of this assay in diagnosing TB in children is predicated on obtaining good quality sputum samples. The utility of Xpert MTB/RIF will be compromised if sputum collection capacity is not improved. Our analysis demonstrates that any expansion in Xpert MTB/RIF use must occur in tandem with concerted efforts to build capacity for improved sputum collection for those children unable to expectorate spontaneously.

This study had several limitations. We were not able to distinguish whether lack of diagnostic capacity was due to lack of human resources or diagnostic hardware. Furthermore, where it was available, we were unable to differentiate the quality, comprehensiveness or availability of diagnostic capacity. Strengths of our study include the large number of sites, which allowed us to conduct an analysis of the availability of pediatric TB diagnostics across several sub-Saharan countries. Given that ICAP provides antiretroviral drugs (ARVs) to approximately 9% of persons on ARVs in eight of the nine countries included,* we believe that our findings are arguably representative of President's Emergency Plan for AIDS Relief (PEPFAR) funded programs from a diverse array of settings and contexts.[9]

## Conclusion

Across 651 pediatric HIV sites in Africa, resources for the diagnosis of TB in children were limited. While 87% of the sites had access to smear microscopy, fewer than 10% had the capacity to procure sputum samples in children unable to expectorate spontaneously. Capacity-building initiatives to improve sputum collection in children are urgently needed.

*Swaziland excluded.

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## Table 1
**HIV care and treatment site characteristics, September 2010 (*N* = 651)**

| | Number of pediatric HIV care and treatment sites *n* (%) | Children aged 0–14 years enrolled in HIV care and treatment* *n* (%) |
|---|---|---|
| Total | 651 | 82 413 |
| Country | | |
| Cote d'Ivoire | 60 (9) | 455 (1) |
| Ethiopia | 62 (10) | 8 145 (10) |
| Kenya | 157 (24) | 15 510 (19) |
| Mozambique | 60 (9) | 23 138 (28) |
| Nigeria | 28 (4) | 2 863 (3) |
| Rwanda | 42 (6) | 3 742 (4) |
| South Africa | 67 (10) | 8 666 (11) |
| Swaziland | 49 (8) | 14 883 (18) |
| Tanzania | 126 (19) | 5 011 (6) |
| Location | | |
| Urban | 128 (20) | 30 987 (38) |
| Semi-urban | 204 (31) | 28 101 (34) |
| Rural | 319 (49) | 23 327 (28) |
| Clinic type | | |
| Primary | 379 (58) | 27 673 (34) |
| Secondary/tertiary | 196 (30) | 50 769 (62) |
| Private/other | 76 (12) | 3 971 (4) |
| Program size (cumulative number of HIV-infected adults and children enrolled in care) | | |
| <352 | 320 (50) | 4 926 (6) |
| ≥352 | 324 (50) | 77 487 (94) |
| Data missing | 7 | 0 |
| Program maturity (years since inception of pediatric HIV services), years | | |
| ≥5 | 50 (8) | 22 735 (28) |
| ≥3–<5 | 155 (24) | 27 616 (34) |
| ≥1–<3 | 358 (55) | 30 855 (37) |
| <1 | 88 (14) | 1 207 (1) |

* Cumulative number enrolled, pre-ART and on ART.

HIV = human immunodeficiency virus; ART = antiretroviral therapy.

**Table 2**

**Bivariate analysis: factors associated with availability of diagnostic tests for diagnosing TB in children at pediatric HIV care and treatment sites in nine countries, September 2010 (*N* = 651)***

| | Smear microscopy | | | Sputum culture | | | Chest X-ray | | |
|---|---|---|---|---|---|---|---|---|---|
| | ***n* (%)** | **PR (95%CI)** | ***P* value** | ***n* (%)** | **PR (95%CI)** | ***P* value** | ***n* (%)** | **PR (95%CI)** | ***P* value** |
| Total pediatric HIV sites | 565 (87) | | | 352 (54) | | | 330 (51) | | |
| Total pediatric patients served by surveyed sites | 80 596 (98) | | | 61 471 (7) | | | 60 967 (74) | | |
| Location | | | | | | | | | |
| Urban | 107 (92) | 1.1 (0.99–1.1) | NS | 78 (67) | 1.2 (1.0–1.4) | NS | 89 (77) | 2.2 (1.8–2.6) | <0.0001† |
| Semi-urban | 174 (83) | 0.96 (0.89–1.0) | NS | 87 (42) | 0.73 (0.60–0.87) | NS | 126 (60) | 1.7 (1.4–2.1) | <0.0001† |
| Rural | 284 (87) | 1.0 | | 187 (57) | 1.0 | | 115 (35) | 1.0 | |
| Facility type | | | | | | | | | |
| Primary | 317 (83) | 1.0 | | 206 (54) | 1.0 | | 137 (36) | 1.0 | |
| Secondary/ tertiary | 189 (98) | 1.2 (1.1–1.2) | <0.0001† | 126 (66) | 1.2 (1.1–1.4) | 0.0059† | 161 (84) | 2.3 (2.0–2.7) | <0.0001† |
| Private/other | 59 (76) | 0.91 (0.80–1.0) | NS | 20 (26) | 0.47 (0.32–0.70) | 0.0002 | 32 (41) | 1.1 (0.85–1.5) | NS |
| Program size (cumulative no. of children and/or adults enrolled) | | | | | | | | | |
| <352 | 244 (76) | 0.97 (0.96–0.98) | <0.0001† | 121 (38) | 0.95 (0.93–0.97) | <0.0001† | 105 (33) | 1.0 | <0.0001† |
| ≥352 | 316 (98) | 1.0 | | 230 (71) | 1.0 | | 224 (69) | 2.1 (1.8–2.5) | |
| Program maturity (years since initiation of pediatric HIV services), years | | | | | | | | | |
| ≥5 | 49 (98) | 1.3 (1.1–1.5) | 0.0004 | 39 (78) | 1.9 (1.4–2.6) | <0.0001 | 44 (88) | 2.8 (2.0–3.8) | <0.0001† |
| ≥3–<5 | 155 (100) | 1.0 (0–0) | NS | 110 (71) | 1.7 (1.3–2.3) | <0.0001† | 113 (73) | 2.3 (1.7–3.2) | <0.0001† |
| ≥1–<3 | 299 (84) | 1.1 (1.0–1.3) | 0.0452† | 167 (47) | 1.1 (0.87–1.50) | NS | 145 (41) | 1.3 (0.91–1.8) | NS |
| <1 | 62 (70) | 1.0 | | 36 (41) | 1.0 | | 28 (32) | 1.0 | |
| Country | | | | | | | | | |
| Cote d'Ivoire | 17 (3) | | | 1 (2) | | | 19 (32) | | |
| Ethiopia | 62 (11) | | | 37 (60) | | | 55 (89) | | |
| Kenya | 147 (26) | | | 135 (86) | | | 58 (37) | | |
| Mozambique | 57 (10) | | | 52 (87) | | | 49 (82) | | |

| | Smear microscopy | | | Sputum culture | | | Chest X-ray | | |
|---|---|---|---|---|---|---|---|---|---|
| | ***n*** **(%)** | **PR (95%CI)** | ***P*** **value** | ***n*** **(%)** | **PR (95%CI)** | ***P*** **value** | ***n*** **(%)** | **PR (95%CI)** | ***P*** **value** |
| Nigeria | 28 (5) | | | 10 (36) | | | 24 (86) | | |
| Rwanda | 42 (7) | | | 31 (74) | | | 15 (36) | | |
| South Africa | 66 (12) | | | 65 (97) | | | 43 (64) | | |
| Swaziland | 37 (7) | | | 10 (20) | | | 9 (18) | | |
| Tanzania | 109 (19) | | | 11 (9) | | | 58 (46) | | |

*The table excludes missing values. Categories are not mutually exclusive. Facilities were able to choose multiple responses.

†Statistically significant.

TB = tuberculosis; HIV = human immunodeficiency virus; PR = prevalence ratio; CI = confidence interval; NS = non-significant.

**Table 3**

**Bivariate analysis: factors associated with reported capacity to procure sputum samples in children at pediatric HIV care and treatment sites in nine countries, September 2010 (*n* = 651)***

| | Naso-pharyngeal aspirate | | | Gastric aspirates | | | Induced sputum | | |
|---|---|---|---|---|---|---|---|---|---|
| | ***n* (%)** | **PR (95%CI)** | ***P* value** | ***n* (%)** | **PR (95%CI)** | ***P* value** | ***n* (%)** | **PR (95%CI)** | ***P* value** |
| Total pediatric HIV sites | 12 (2) | | | 34 (5) | | | 39 (6) | | |
| Total pediatric patients served by surveyed sites | 3 814 (5) | | | 11 236 (14) | | | 7 729 (9) | | |
| Location | | | | | | | | | |
| Urban | 6 (5) | 16.9 (2.1–138.6) | 0.0086† | 14 (12) | 3.9 (1.8–8.6) | 0.0006† | 7 (6) | 1.0 (0.43–2.3) | NS |
| Semi-urban | 5 (2) | 7.8 (2.1–66.3) | 0.0599† | 10 (5) | 1.6 (0.66–3.7) | NS | 12 (6) | 0.94 (0.47–1.9) | NS |
| Rural | 1 (0.3) | 1.0 | | 10 (3) | 1.0 | | 20 (6) | 1.0 | |
| Facility type | | | | | | | | | |
| Primary | 5 (1) | 1.0 | | 14 (4) | 1.0 | | 12 (3) | 1.0 | |
| Secondary/tertiary | 7 (4) | 2.8 (0.89–8.6) | NS | 19 (10) | 2.7 (1.4–5.3) | 0.0037† | 24 (13) | 4.0 (2.0–7.8) | <0.0001 |
| Private/other | 0 | — | — | 1 (1) | 0.35 (0.05–2.6) | NS | 3 (4) | 1.2 (0.35–4.2) | NS |
| Program size (cumulative no. of children and/or adults enrolled) | | | | | | | | | |
| <352 | 2 (1) | 4.9 (1.1–22.4) | 0.038† | 8 (3) | 1.0 | | 14 (4) | 1.0 | |
| ≥352 | 10 (3) | 1.0 | | 26 (8) | 3.2 (1.5–7.0) | 0.0033† | 25 (8) | 1.8 (0.93–3.3) | NS |
| Program maturity (years since initiation of pediatric HIV services), years | | | | | | | | | |
| ≥5 | 8 (16) | | | 9 (18) | 5.3 (1.5–18.6) | 0.0096 | 8 (16) | 1.8 (0.70–4.4) | NS |
| ≥3–<5 | 3 (2) | | | 10 (6) | 1.9 (0.53–3.7) | NS | 10 (6) | 0.71 (0.29–1.7) | NS |
| ≥1–<3 | 1 (0) | | | 12 (3) | 1.0 (0.28–3.4) | NS | 13 (4) | 0.40 (0.17–0.93) | 0.0342† |
| <1 | 0 | | | 3 (3) | 1.0 | | 8 (9) | 1.0 | |
| Country | | | | | | | | | |
| Cote d'Ivoire | 1 (2) | | | 0 | | | 0 | | |
| Ethiopia | 0 | | | 0 | | | 15 (24) | | |
| Kenya | 0 | | | 2 (1) | | | 11 (7) | | |
| Mozambique | 3 (5) | | | 4 (7) | | | 2 (3) | | |
| Nigeria | 1 (4) | | | 3 (11) | | | 1 (4) | | |

| | Naso-pharyngeal aspirate | | | Gastric aspirates | | | Induced sputum | | |
|---|---|---|---|---|---|---|---|---|---|
| | ***n*** **(%)** | **PR (95%CI)** | ***P*** **value** | ***n*** **(%)** | **PR (95%CI)** | ***P*** **value** | ***n*** **(%)** | **PR (95%CI)** | ***P*** **value** |
| Rwanda | 3 (7) | | | 8 (19) | | | 3 (7) | | |
| South Africa | 3 (4) | | | 14 (21) | | | 3 (4) | | |
| Swaziland | 0 | | | 2 (4) | | | 2 (4) | | |
| Tanzania | 1 (1) | | | 1 (1) | | | 2 (2) | | |

*The table excludes missing values. Categories are not mutually exclusive. Facilities were able to choose multiple responses.

†Statistically significant.

TB = tuberculosis; HIV = human immunodeficiency virus; PR = prevalence ratio; CI = confidence interval; NS = non-significant.