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Original Article

Coverage and predictors of pediatric index case testing (ICT) among children of HIV infected parent(s), analysis of population HIV impact assessment (PHIA) surveys

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Abstract

Background: *Antiretroviral therapy (ART) coverage in many Sub-Saharan African countries remains low (48%) for children <15 years living with HIV. One possible reason for this low performance is low pediatric HIV case finding. In this study we describe the coverage of HIV testing for children of infected parent(s) (also called index case testing or ICT) and factors affecting it.*

Methods: *Secondary analysis of the Zambia, Malawi, Eswatini, and Tanzania Population HIV Impact Assessment (PHIA) household surveys which were conducted between 2015-2016 were used for this study. Couples , where there is at least one HIV-infected person, were identified and matched to their children <15 years. HIV testing status of children was measured and factors associated with the testing of children were studied using logistic regression. Sampling weights were applied during analysis taking into account the complex sampling design of these surveys.*

Results: *3,435 children <15 years had at least one infected parent. Of those children, 38.9% (32.9%-44.8%) were tested for HIV. Rural areas had more undiagnosed children in all study countries. Maternal HIV testing was associated with the highest odds of testing for children (adjusted Odds ratio: 84.51 (10.72-666)) as was maternal HIV infection (Odds ratio: 5.9 (95% confidence interval (CI): 3.9-8.9)).*

Conclusion: *Pediatric HIV testing for children of HIV infected parent(s) was found to be low. Maternal HIV testing was found to be the single most important factor associated with testing of children of HIV infected parent (s). Rural settings need to be prioritized for ICT in order to address testing gap.*

Key Words: *Pediatric HIV; Index case testing (ICT); PHIA*

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Background

The progress to diagnose 90% of HIV infected adults and put them on treatment has been going well in many PEPFAR-supported sub-Saharan African countries according to UNAIDS with reported treatment coverage of 60%-90% for adults (1). For children, however, the coverage is much lower at an estimated <50% looking at PEPFAR report, and SPECTRUM modeling data (2, 3).

The consequence of undiagnosed and untreated children is detrimental as most end-up having increased morbidity and mortality from opportunistic infections (4). This means around 50% will die before their second birth day (5). A number of factors were identified as contributory for this low treatment coverage. The most important of these factors is low testing and detection of children.

Index case HIV testing (ICT) for children, which is testing of children of HIV infected parent(s), is the most important HIV case finding modality that leads to identification of infected children at high positivity rate (6). It is also associated with early case finding (7).

Even though ICT is the preferred option to identify undiagnosed children, there are several factors leading to the approach not being used optimally. Individual factors included dependence of children on adults for testing (8), caregiver related factors like sense of guilt (9), fear of stigma (10), fear of inadvertent disclosure of HIV status (11), fear of positive result (12), and health system factors like lack of experience with pediatric testing, health care workers considering children low risk, and work load (11, 13). None of these studies have identified individual children and parental socio-demographic factors including HIV testing and infection status as determinants. This study will therefore determine coverage of index case testing (ICT) among children of HIV infected parents and identify determinants at individual level.

Materials and Methods

Study setting and design

Secondary analysis of four Population HIV Impact Assessment (PHIA) studies conducted in Eswatini, Malawi, Tanzania and Zambia are used in this study. These are household surveys with two stage stratified cluster sampling design. Within selected households, a structured questionnaire was used to interview and collect response on variables of interest. Refer to PHIA survey methodologies for the detail. (14) We used a cross-sectional study design to answer the study questions.
Study period: All surveys were conducted from 2015-2016.

Inclusion criteria

all children <15 years who have matching biological parents who consented for home based HIV testing and structured interview were included.

Sample size

taking HIV testing among children <15 for parents where there is at least one HIV infected parent at 50%, acceptable difference of 0.05, assuming design effect of 2, and 901 clusters sampled in the four surveys, a sample size required becomes 768. After inclusion criteria, a sample size of 3,435 was obtained and all were included in the analysis.

Outcome variable

HIV testing status of children <15 years. We also analyzed reason for not getting HIV testing.
Independent variables: child age, child gender, parental gender, parental age, parental education status, wealth status, residence, HIV testing status of parents, HIV infection status of parents, and ART treatment status.

Operational definition

HIV testing: tested for HIV irrespective of being HIV+ or HIV- or being aware of their HIV+ status.

HIV infection: being HIV+ irrespective of HIV testing or awareness of HIV+ status.
Awareness of HIV+ status: knowing HIV+ status. Some people may have tested for HIV in the past while they were HIV negative. Currently they may be HIV infected but may not know they have HIV infection.

ART treatment status: being HIV positive and on antiretroviral therapy.

HIV/ART status: measure of combination of HIV testing, HIV infection, awareness of HIV+ status, and ART treatment status. Here are sub-categories of this variable:

- Not infected, not tested: HIV negative but had never tested for HIV.
- Not infected, tested: HIV negative and had been tested for HIV.
- HIV+ status unknown: HIV positive but status not known whether tested for HIV in the past or not.
- Known+, not on ART: HIV+ and aware of HIV infection status but the person is not on ART.
- Known+, On ART: HIV+ and aware of HIV infection status and on ART.

Data analysis

Stata Version 14.0 statistical software was used for analysis. Sampling weights were applied during calculation of descriptive (frequency, proportion, and mean), and inferential (logistic regression) statistics to measure ICT coverage and identify its determinants taking into account complex sampling design used in PHIA surveys. The role of HIV/ART status in determining ICT coverage of children was analyzed as primary predictor using logistic regression. In addition, each of the following variables was assessed for association with ICT coverage using logistic regression:

- maternal HIV testing, and paternal HIV testing, which were modeled together;
- maternal HIV infection, and paternal HIV infection, which were modeled together;
- awareness of HIV+ status by the mother modeled separately from awareness of HIV+ status by the father as the two subset data don't have identical couples;
- ART treatment status of the mother modeled separately from ART treatment status of the father modeled separately as the two subset data don't have identical couples.

Purposeful selection of variables was used during regression model building. Those with p-value <0.20 during bi-variable analysis were included in the final model. Level of significance was set at 0.05. Pie chart and bar graphs were used to graphically show coverage of testing or gaps. Finally, frequency and percentage were used to describe why children did not receive index case testing.

Ethics statement: This study was done based on secondary analysis of existing data. No human subjects were involved in the study. All databases don't have individual identifiers like names or addresses that can be used to identify people. All PHIA surveys received ethical approval from the institutional review boards of CDC, Columbia University, Westat, the National Institute for Medical Research, and respective country's research and ethics committee before initiation of data collection (14).

Results

Of 13,212 couples included in the surveys, 1,570 had at least one person infected with HIV with a total of 3,435 children (50.9% female, 44.5% under five years, and 34.9% living in urban residence). The average number of children was 2.01 (95% confidence interval (CI): 1.92 -2.09) and 2.36 (95% CI: 2.28-2.44) children per couple with at least one infected parent in urban and rural settings, respectively.

Coverage of ICT

ICT coverage for children <15 years of age born to HIV infected parent(s) varied across different countries with the highest being for Eswatini at 69.8%. The majority undiagnosed children <15 years were located in rural settings, the highest being for Malawi at 83% and the lowest in Zambia at 59.5% (Figure 1)

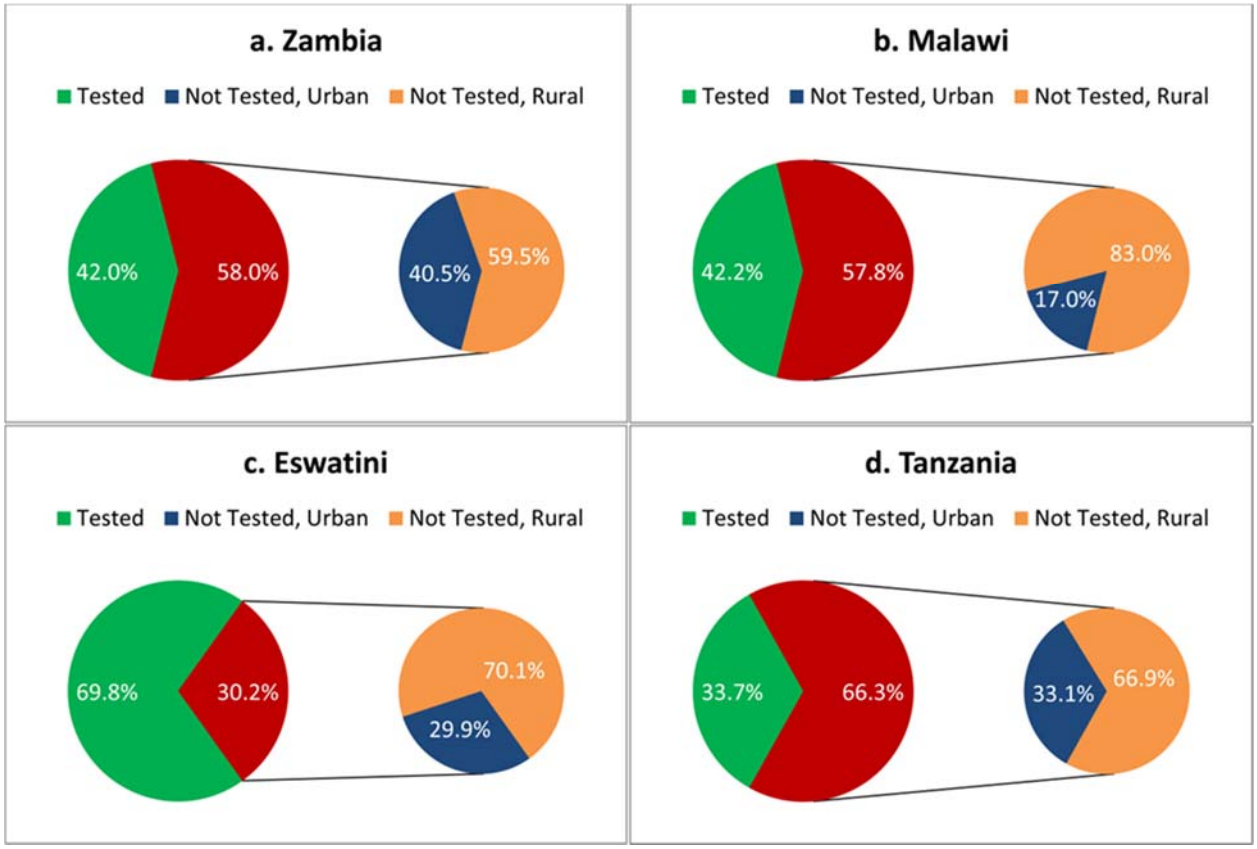

Figure 1. Index Case Testing Coverage by Country and Urban/Rural Settings, by Country:
a. Zambia (tested n=430, not tested n=595, not tested urban n=241, not tested rural=354);
b. Malawi (tested n=417, not tested n=571, not tested urban n=97, not tested rural=474);
c. Eswatini (tested n=397, not tested n=172, not tested urban n=51, not tested rural=121);
d. Tanzania (tested n=192, not tested n=377, not tested urban n=125, not tested rural=252);

Determinants of Coverage of ICT

Looking at determinants of ICT coverage for children <15 years, age of a child and HIV/ART status of the mother (as per operational definition) were found to be independent predictors. Older children (age >5 years old) were found to have lower HIV testing rate, 31.7%, compared to younger children (≤5 years), 47.8% (p value <0.001). Compared to couples where the mother was HIV negative and was never tested (while the father was HIV infected), odds ratio of testing of children was 17.4 (95% CI: 2.4-127.0) when the mother was tested and HIV negative, 15.1 (95% CI: 1.9-120.9) when the mother was infected but status was unknown, 57.5 (95% CI: 7.0-470.5) when the mother was known to be infected but not on ART, and 158.6 (95% CI: 21.4-1178.7) when the mother was infected and on ART. (see Table 1 above)

Table 1. Determinants of HIV Testing among Children <15 years Born to Couples at least one of whom has HIV, data from Four PHIA Surveyed Countries (Zambia, Malawi, Eswatini, and Tanzania), 2015-2016.

Variable	Response	Total n <15 Children	n (%) <15 Children Tested	Odds ratio (95% CI)	P value	Adjusted Odds ratio (95% CI)
Child's Gender	Male	1,688	622 (36.8%)	1	0.305	
	Female	1,747	714 (40.9%)	1.19 (0.85-1.66)		
Child's Age	0-2	733	361 (49.2%)	1	0.002	1
	3-5	795	370 (46.6%)	0.9 (0.59-1.37)		0.97 (0.65-1.45)
	6-10	1,046	294 (28.1%)	0.4 (0.26-0.63)		0.41 (0.25-0.66)
	11-14	861	310 (36.0%)	0.58 (0.34-0.99)		0.59 (0.35-0.99)
Residence	Urban	1,198	555 (46.3%)	1	0.068	
	Rural	2,237	780 (34.9%)	0.62 (0.37-1.04)		
Maternal Age	≤40	1,880	780 (41.5%)	1	0.532	
	41-50	1,194	420 (35.2%)	0.77 (0.48-1.23)		
	>50	361	135 (37.4%)	0.84 (0.36-1.99)		
Paternal Age	≤40	1,575	660 (41.9%)	1	0.422	
	41-50	1,433	502 (35.0%)	0.75 (0.48-1.17)		
	>50	428	173 (40.5%)	0.94 (0.44-2.02)		
Maternal Education	Illiterate	634	257 (40.5%)	1	0.168	
	Primary	2,280	830 (36.4%)	0.84 (0.37-1.92)		
	Secondary	477	223 (46.7%)	1.28 (0.54-3.03)		
	Tertiary	44	25 (58.3%)	2.04 (0.59-7.04)		
Paternal Education	Illiterate	374	93 (25.0%)	1		
	Primary	2,073	783 (37.8%)	1.82 (0.59-5.62)	0.005	
	Secondary	865	378 (43.7%)	2.34 (0.72-7.61)		
	Tertiary	122	80 (65.7%)	5.77 (1.66-20.1)		
Wealth of Household	Lowest	662	207 (31.3%)	1	0.014	
	Lower	698	168 (24.1%)	0.70 (0.29-1.69)		
	Middle	806	374 (46.4%)	1.90 (0.78-4.59)		
	Higher	800	324 (40.5%)	1.49 (0.65-3.42)		
	Highest	469	262 (55.8%)	2.77 (1.19-6.47)		
Maternal HIV Status	Not infected not tested	174	2 (1.1%)	1	<0.001	1
	Not infected tested	1016	179 (17.6%)	18.67 (2.56-136.24)		17.49 (2.41-127.02)
	HIV+ status unknown	545	82 (15.1%)	15.56 (1.97-123.13)		15.13 (1.89-120.89)
	Known+ not on ART	146	59 (40.2%)	58.87 (7.36-471.18)		57.49 (7.02-470.52)
	Known+ on ART	1553	1013 (65.2%)	164 (22.24-1208.64)		159 (21.35-1178.68)
Paternal HIV Status	Not infected not tested	149	66 (44.2%)	1	0.007	
	Not infected tested	703	364 (51.7%)	1.34 (0.53-3.39)		
	HIV+ status unknown	1166	251 (21.5%)	0.34 (0.13-0.92)		
	Known+ not on ART	224	138 (61.7%)	2.01 (0.65-6.24)		
	Known+ on ART	1192	517 (43.4%)	0.96 (0.40-2.34)		

Figure 2 summarizes the relationship between maternal and paternal HIV status on ICT coverage. ICT coverage was high for children of mothers on ART irrespective of HIV infection, testing or treatment status of partner (59%-87%). For HIV+ mothers not on ART, testing of their children was also relatively high when the father was infected irrespective of testing or ART treatment status (45%-66%). When the mother was infected but not tested, ICT for children was generally ≤21%. ICT coverage was ≤18% when the father was infected but mother was HIV negative.

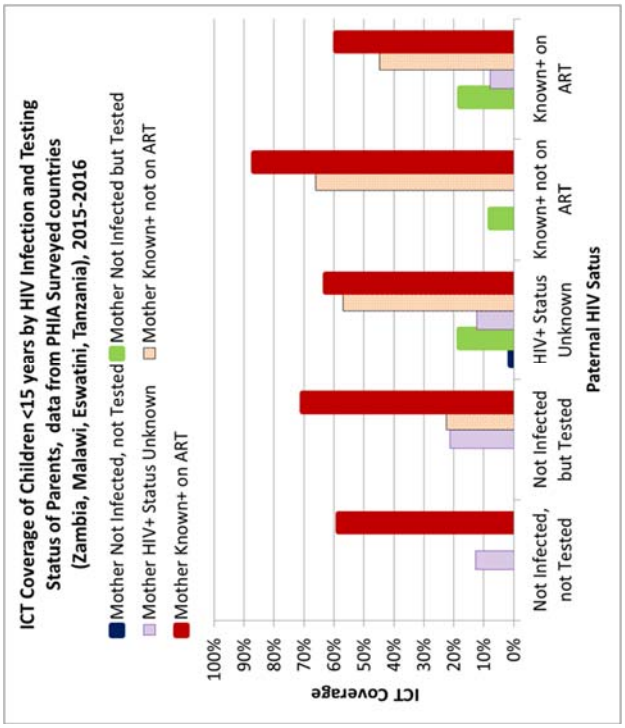

Figure 2. ICT Coverage of Children by HIV Infection, Testing, and Treatment Status of Parents, data from Four PHIA Surveyed Countries (Zambia, Malawi, Eswatini, and Tanzania), 2015-2016.

ICT coverage was high for children of mothers on ART irrespective of HIV infection, testing or treatment status of partner (59%-87%). For HIV+ mothers not on ART, testing of their children was also relatively high when the father was infected irrespective of HIV testing or treatment status. (45%-66%) When the mother was infected but not tested, ICT for children was ≤21%. ICT coverage was ≤18% when the father was infected but mother was HIV negative.

Looking at individual predictors, maternal HIV testing was a significant predictor of testing for children (odds ratio 84.5; 95% CI: 10.7- 666.2) irrespective of HIV infection status of the mother and HIV testing status of the father. Maternal HIV infection was also a predictor of children irrespective of paternal HIV testing of infection status. Both maternal and paternal awareness of HIV+ status were predictors of testing of children: odds ratio 9.42 (5.55-16.0) and 3.2 (2.1-4.8), respectively. Finally, for HIV+ mothers, being on ART was associated with better testing of children (odds ratio 2.8; 95% CI 1.4-5.7). For HIV+ fathers, being on ART was not associated with improved testing of children. (Table 2)

Table 2. Independent Predictors of ICT Coverage among children born to Parent(s) with HIV, data from Four PHIA Surveyed Countries (Zambia, Malawi, Eswatini, and Tanzania), 2015-2016

Variable	Response	Number of <15 Children	Number of <15 Children Tested (%)	Adjusted Odds ratio*	P value
Mother tested for HIV	No	310	2 (0.6%)		
	Yes	3,125	1333 (42.7%)	84.51 (10.72-666)	<0.001
Mother HIV+	No	1,191	181 (15.2%)		
	Yes	2,244	1154 (51.4%)	5.91 (3.91-8.94)	<0.001
Mother aware of HIV+ status	No	588	89 (15.1%)		
	Yes	1,831	1155 (63.1%)	9.42 (5.55-16.0)	<0.001
Father aware of HIV+ status	No	1,158	249 (21.5%)		
	Yes	1,407	650 (46.2%)	3.16 (2.08-4.82)	<0.001
Mother on ART if HIV+	No	168	68 (40.3%)		
	Yes	1,794	1170 (65.2%)	2.78 (1.35-5.73)	0.008

*** Adjusted for socio-demographic factors**

As for the reason why children were not tested for HIV when at least one parent was infected, 58.7% stated that the child didn't need testing followed by 23.4% saying they were very far from testing site (n=652).

ICT Burden for Children of HIV+ mothers

Figure 3 shows ICT burden for children of HIV infected mothers that still needed HIV testing by maternal HIV diagnosis and ART treatment status. Of children who still needed ICT, 50% were children of HIV+ mothers on ART, while 42% were children of undiagnosed HIV+ mothers. A minority 8% children were born to HIV+ mothers who knew their HIV positive status but weren't on ART (n=2120).

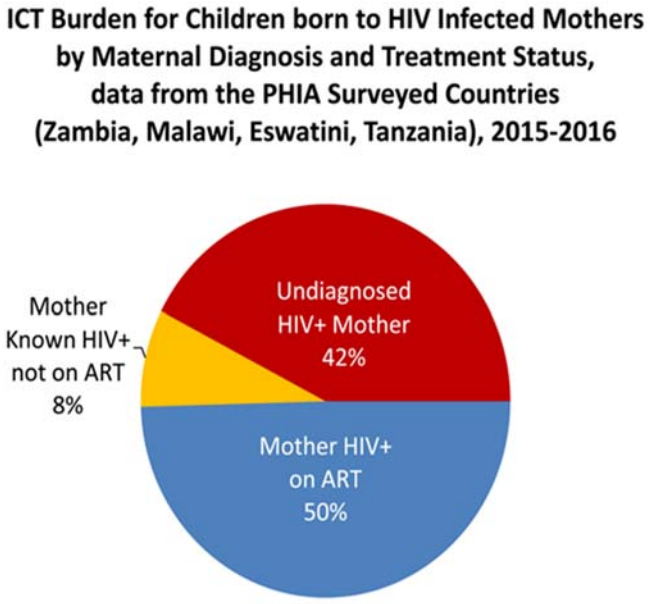

Figure 3. ICT Burden for Children born to HIV Infected Mother by Maternal Diagnosis and Treatment Status, data from the PHIA Surveyed Countries (Zambia, Malawi, Eswatini, Tanzania), 2015-2016.

This figure indicates of children born to HIV+ mothers and were never tested for HIV, 50% had HIV+ mother on ART while 42% had a mother never tested for HIV herself. (n=1090)

Discussion

Pediatric HIV case finding using index case testing was found to be low in all study settings except for Eswatini. Among parents who responded to the question why a child was not tested for HIV, the majority responded as the child didn't need the test. This is a troubling pattern and needs to be addressed through counseling.

Other factors for low ICT performance may include failure of health care workers to provide HIV testing, and low access for early infant diagnosis and each need to be addressed (11, 15-17). Line listing, tracking and testing of eligible children from ART sites, training support for health care workers and support staff, strong monitoring, supervision and coaching focusing on ICT may strengthen health systems (18). At individual level, the use of HIV self-test, home based or community based testing can facilitate testing for children by bringing testing closer to the family (19). This will help to address gaps in testing arising from the need to travel long distance for testing. Offering weekend testing services is another option as eligible children often go to school during normal office hours (15).

All possible entry points at facility and community level need to be explored to minimize missed opportunities for ICT (20, 21). That is why addressing gaps in HIV testing needs to be addressed urgently. However, the low hanging fruit still is ART clinics that serve infected parents on treatment (22). Equally important for pediatric HIV case finding is parental HIV testing as nearly 50% undiagnosed children have undiagnosed parents as indicated in this study. Prioritizing targeted testing of parents in settings providing service for children and adolescents may be needed (23).

ICT seems to be prioritized when there is maternal infection. This is logical as mother to child transmission accounts for the majority of pediatric infection as high as >90%. But, that should not be the only consideration for testing as there is a possibility of transmission from the father through the sharing of sharp objects within a household (24). In addition, the first index identified may be the father, in which case children should be tested without delay irrespective of maternal testing (25).

Maternal testing was found to be the driving force for testing of children irrespective of whether the mother was infected or not. It is therefore important to make use of this in testing of at risk children using family centered approach. Additionally, testing of children was found to be better when mothers knew their HIV+ status. Testing of children was even better when the mother was on ART. Only when fathers knew their HIV+ status did more children got tested compared to those who didn't know their HIV+ status. Even in that case, however, ICT for children was average. That needs to alert health care workers that counseling

including disclosure support needs to be very good when the index is the father (26).
Access for testing may be an issue as most children who were not tested were found to be in rural settings. This needs a strategic approach if the first 95 and second 95 targets are to be met for children. PEPFAR's pivot to high burden settings means mostly urban areas with high HIV burden are targeted (3). Rural settings still need to have targeted interventions like ICT taking into consideration cost of interventions (27, 28).

Looking at age of children, older children were found to be less likely to be tested. This may be due to low perception of the possibility of infection in older children (29). Late progression is a strong possibility especially when the infection occurs late through breast feeding (30). The other possibility is that parents may have false sense of security if PMTCT interventions were received. The determination of final infection status of HIV exposed infants at 12-18 months is an important intervention that should be strengthened. Current trends in Kenya, for instance, show that final status is not determined in 22% of children even after receiving PMTCT interventions (31).

Counseling approaches need to take literacy into account since (15), tertiary education of the father was associated with better ICT coverage. Index parents from highest wealth quintile were associated with low ICT coverage. Wealthy people usually take treatment in private facilities which should be targeted to reach them (32).

The analysis in this study focused on testing of children at least once. As stated earlier, there always is a possibility of infection outside the mother-to-child transmission window and hence, the testing gap reported here shows the minimum. Parents should be educated of this risk and HIV risk assessment conducted on ongoing basis to identify and test eligible children (33).

This study quantified one of the root causes for the low pediatric ART up take in many sub-Saharan African countries which is low pediatric case finding due to low ICT coverage. Important determinants like the role of PMTCT knowledge on ICT coverage, for instance, can be explored in demographic health surveys but these surveys need to measure pediatric HIV testing as a variable (34). Studies are also needed to explore why children eligible for ICT are not tested to design targeted and individualized interventions. The most important limitation of this study was that reason for not getting children tested was not captured for all parents and hence we couldn't present the complete picture.

Conclusion

Pediatric HIV testing for children of HIV infected parent(s) was found to be low. Maternal HIV testing was found to be the single most important factor to get a child tested for HIV. There still are missed opportunities in ICT testing of children even when parents know their HIV+ status and that should be addressed urgently. Rural settings need to be prioritized for ICT in order to address testing gap. Adult case finding is as important for pediatric HIV case finding as nearly half children who need testing are living with undiagnosed mothers.

Conflict of interest: None

Author contribution: KD conceived the idea, designed the methodology, did analysis and write up.

Consent to Publish: Not applicable

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