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Recent HIV Infection Surveillance in Routine HIV Testing in Nairobi, Kenya: A Feasibility Study

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Background: Serological tests can distinguish recent (in the prior 12 months) from long-term HIV infection. Integrating recency testing into routine HIV testing services (HTS) can provide important information on transmission clusters and prioritize clients for partner testing. This study assessed the feasibility and use of integrating HIV recency into routine testing.

Methods: We conducted a multi-method study at 14 facilities in Kenya, and key informant interviews with health care providers. We abstracted clinical record data, collected specimens, tested specimens for recent infection, returned results to participants, and conducted a follow-up survey for those recently infected.

Results: From March to October 2018, we enrolled 532 clients who were diagnosed HIV-positive for the first time. Of these, 46 (8.6%) were recently infected. Women aged 15–24 years had 2.9 (95% confidence interval: 1.46 to 5.78) times higher adjusted odds of recent infection compared with 15–24-year-old men and those tested within the past 12 months having 2.55 (95% confidence interval: 0.38 to 4.70) times higher adjusted odds compared with those tested

≥12 months previously. Fourteen of 17 providers interviewed found the integration of recency testing into routine HTS services acceptable and feasible. Among clients who completed the follow-up interview, most (92%) felt that the recency results were useful.

Conclusions: Integrating recent infection testing into routine HTS services in Kenya is feasible and largely acceptable to clients and providers. More studies should be done on possible physical and social harms related to returning results, and the best uses of the recent infection data at an individual and population level.

Key Words: HIV testing, HIV incidence, recent infection testing algorithm, limiting antigen avidity enzyme immunoassay, sub-Saharan Africa

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INTRODUCTION

UNAIDS has set global goals for 95% of all people living with HIV (PLHIV) to be diagnosed, 95% of these to be initiated and retained on antiretroviral therapy (ART), and 95% of these to be virally suppressed (95-95-95) by 2030 (see Supplemental Digital Content 1, <http://links.lww.com/QAI/B439>).¹ Achieving 95% diagnosis will require new approaches to maximize case finding. One such approach is the latent antigen avidity assay for recent HIV infection.^{2–6} When used in combination with viral load (VL) testing [ie, the recent infection testing algorithm (RITA)], it can identify persons whose infection occurred within the last 12 months.^{7–12} These assays can be integrated into HIV surveillance systems and testing programs to identify groups with high incidence, characterize current risk factors for infection, and target hot spots of transmission among the hardest-to-reach populations, and through contact tracing identify PLHIV who have not been diagnosed, PLHIV who have fallen out of care, and uninfected individuals at high risk of infection who may benefit from pre-exposure prophylaxis.⁵

Integrating RITA, which pairs recency and VL assays, and where possible antiretroviral (ARV) metabolite testing, to minimize the false recency rate^{11,12} into HIV testing and counseling (HTC) services, has been proposed as a means to identify geographic areas and populations with ongoing transmission to better target prevention programs and index testing efforts.¹⁴ However, before scale-up, national HIV programs need to evaluate the risks

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and benefits of conducting recency testing and whether there is an ethical obligation to return results to clients. More data are needed on potential harms of knowing recent infection status and whether there are increased rates of intimate partner violence or other social harms related to disclosing recent HIV status compared with disclosing HIV infection in general. In addition, facilities will need to determine how to use recency test results to support partner notification. The use should be evaluated in light of the added costs and time related to recent infection testing in routine HTC.

We assessed the acceptability and feasibility of integrating recency testing into routine HTC services and identified and characterized recent HIV infections among newly-diagnosed clients attending HTC services Eastern Deanery AIDS Relief Programme (EDARP) facilities in Nairobi, Kenya.¹⁵

METHODS

Clients presenting for routine HTC at all 14 EDARP facilities were screened for eligibility. We invited clients who were ≥ 15 years old and had received an HIV-positive result for the first time between March and October 2018 to participate. Informed consent was administered in English or Swahili. Those who declined consent proceeded with treatment per national guidelines. Health care providers returned RITA results and provided post-test counselling to participants and at a subsequent visit, administered a follow-up survey on partner notification and testing, intimate partner violence, and initiation of ART to participants with recent infections. All persons testing HIV-positive were encouraged to refer partners for HIV testing through index testing, per standard of care.

Once consent was obtained, we collected 6.0 mL of venous blood in an EDTA tube and pipetted samples onto 2 Whatman 903 Snap-Apart Cards with 5 dried blood spots of 70 μL each, for a total of 10 filled spots per participant. We abstracted demographic and clinical variables from each participant's electronic health record. Testing for recent infection was performed using RITA that combined the limiting antigen avidity enzyme immunoassay (LAG Avidity EIA) (Maxim Biomedical, Rockville, MD) VL testing, and ARV metabolite testing to confirm classification of recent infections. The LAG testing protocol requires the assay to be performed twice. Specimens with an ODn value of ≤ 1.5 were confirmed by further testing of the samples. The ODn is calculated by dividing the optical density (OD) for each specimen by the median OD of the calibrator. We measured HIV-1 RNA VL using the Abbott m2000, Roche Cobas Ampliprep/Cobas TaqMan (Roche Diagnostics USA, Indianapolis, IN). Specimens in which VL was ≤ 1000 copies/mL were classified as "long-term" infections, irrespective of the assay result. Specimens in which VL was > 1000 copies/mL and ODn ≤ 1.5 were classified as "recent" infections, ie, infections acquired in the prior 12 months. Because prior ARV exposure affects the accuracy of the LAG assay, we also tested samples classified as recent infections for the presence of efavirenz, nevirapine, atazanavir, and lopinavir metabolites in the blood. Qualitative detection of ARV drugs was performed on LAG-positive samples using high-performance liquid chro-

matography coupled with tandem mass spectrometry. Samples above the lower limit of detection ($< 0.02 \mu\text{g/mL}$) for any of the ARV drugs tested were classified as ARV-positive. VL testing was conducted at the EDARP laboratory in Nairobi, LAG testing was conducted at the National HIV Reference Laboratory in Nairobi, and ARV metabolite testing was conducted at the University of Cape Town in South Africa.

We performed multivariable logistic regressions to examine associations between predictor variables and recent infection using STATA 14.2 (Stata Corporation, College Station, TX). In the final model, we retained variables that had a *P*-value less than 0.05. We disaggregated the final model by gender.

Qualitative Analysis

We also conducted key informant interviews with purposively selected health care providers from EDARP facilities in November 2018 using a semi-structured interview guide. We reviewed audio recordings of interviews 3 times. A summary was developed for each interview, which included illustrative quotes we transcribed verbatim. We used a coding scheme, based on the interview guide, to code all interviews and classical content analysis to analyze the data.

Participants including key informants provided consent before participating in the study. The study was approved by ethical review boards at the University of California, San Francisco, the Kenyatta National Hospital, the London School of Hygiene and Tropical Medicine and EDARP.

RESULTS

A total of 883 persons tested positive for HIV at the 14 study sites. Of those, 255 had previously tested positive and were, therefore, ineligible. Ninety-six did not consent to participate; 532 were eligible, consented to participate, and enrolled in the study (Fig. 1).

Four hundred seventy participants (88%) had an ODn value of > 1.5 , and were accordingly classified as long-term infections. Sixty-two participants (12%) had an ODn value of ≤ 1.5 and required VL testing to confirm the recency classification; of those, 12 (22%) were classified as long-term after VL testing; 2 participants had insufficient volume for VL testing and were excluded. Of the 62 participants, 48 (77%) were classified as recent per the RITA and sent for ARV metabolite testing; 2 (4%) had ARV metabolites present and were reclassified as long-term infections. Thus, 46 (9%) of all participants tested and 71% of those initially positive on LAG avidity assay were classified as recent after all confirmatory tests were completed.

A higher proportion of recent infection was found among women [adjusted odds ratio (aOR) = 4.20, *P* < 0.001], those under 25-years-old (aOR = 3.55, *P* < 0.001), and those who had been tested in the prior 12 months (aOR = 2.55, *P* < 0.001). Testing for interactions revealed an interaction between age at diagnosis and gender. As noted in the Table 1, 15-to-29-year-old women had 2.9 times higher adjusted odds of recent infection than men in the same age group.

Of the 532 participants, 402 (76%) received their results; 29 (61%) of the 46 recently infected participants received their results. Of those, 13 (46%) completed the follow-up



FIGURE 1. Study client flow chart.

questionnaire. Overall, clients who received a recent HIV test result found recency testing to be acceptable and clinically useful. A large majority (92%) of participants reported that the recency result encouraged them to seek treatment sooner than they would have otherwise and in particular liked getting their VL results to monitor how they were doing. Ten participants (76.9%) also reported telling at least one sexual partner to be tested for HIV; of these, 6 presented at the site for HIV testing. Four participants (31%) reported experiencing violence or stigma after getting their results, and a little over half (54%) reported that the result had a negative impact on their relationships. There was, however, no way to disentangle negative experiences related to HIV status and recency status disclosure. In most of the cases, the harm came before the recency results were returned, suggesting that it was related to HIV status disclosure and not recency status. Of the 19 participants who tested positive for recent infection and did not receive results, 7 were lost to follow-up, 5 travelled out of Nairobi and did not return, and 7 said they did not want to receive results.

Partner Notification

One hundred forty-four (27%) of newly diagnosed participants (both with recent and long-term infection) brought sexual partners to be tested. Two participants brought 2 partners. Of the 48 recently infected clients, 13 referred 13 partners (0.27 partners/index patient), and of the

482 clients with long-term infection, 131 referred 133 partners (0.27 partners/index patient). Of the 146 index partners referred, 31 (21%) were newly diagnosed with HIV infection; 30 (21%) had been previously diagnosed. Five (39%) of 13 partners of clients with recent infection were found to be HIV infected, 80% of them (4 of 5) were unaware of their status. On the other hand 56 (44%) of 133 partners of clients with long-term infection were found to be HIV infected and 48.2% (27 of 56) were unaware of their status ($P = NS$). Of the 31 partners newly diagnosed with HIV infection, twenty-one consented to recency testing; 5 (23.8%) had recent infection. HIV seroprevalence among partners was 25 times that of routine testing of individuals through HTS (42% compared to 1.7%).

Acceptability and Feasibility of Integrated Recent Infection Testing into HTC

Seventeen EDARP health care providers were interviewed. Fourteen indicated that recent infection testing was acceptable and feasible.¹ Identified benefits included improved ART adherence, more effective treatment monitoring, increased partner notification, and strengthened client-provider rapport. Providers did not report any adverse events related to the study, although they acknowledged the potential for testing results to instigate conflict or violence. One provider recounted her experience with

TABLE 1. Predictors of Recent Infection and Predictors of Recent Infection Disaggregated by Gender*

| | Recent (N = 46) | | | | | | Female | | |
|--|-----------------|---------|------|---------------|------|---------------|--------|------|---------------|
| | N | Percent | OR | 95% CI | aOR | 95% CI | N | aOR | 95% CI |
| Sex | | | | | | | | | |
| Male | 7 | 3.2% | — | — | | | | | |
| Female | 39 | 12.3% | 4.20 | 1.80 to 9.60† | 2.82 | 1.19 to 6.69† | | | |
| Age range | | | | | | | | | |
| 15–24 | 21 | 18.4% | 3.55 | 1.90 to 6.60† | 2.57 | 1.33 to 4.95† | 21 | 2.90 | 1.46 to 5.78† |
| 25+ | 25 | 19.1% | — | — | | | 18 | — | — |
| Reside in catchment area | | | | | | | | | |
| Yes | 41 | 9.0% | 1.45 | 0.55 to 3.80 | | | | | |
| No | 5 | 6.4% | | | | | | | |
| Highest level of education | | | | | | | | | |
| Primary or none | 18 | 6.5% | 0.55 | 0.30 to 1.0 | | | | | |
| Secondary and above | 28 | 11.1% | — | — | | | | | |
| Tested for HIV in last 12 months | | | | | | | | | |
| Yes, tested for HIV within last 12 months | 25 | 14.0% | 2.55 | 1.38 to 4.70† | 2.13 | 1.13 to 4.00† | 16 | 2.35 | 1.18 to 5.78† |
| No, did not test for HIV within last 12 months | 21 | 6.0% | — | — | | | 23 | — | — |
| Pregnancy status (n = 316) | | | | | | | | | |
| Pregnant | 10 | 17.5% | 1.69 | 0.77 to 3.70 | | | | | |
| Not pregnant | 29 | 11.2% | — | — | | | | | |

*A strong interaction between gender and age was observed (*P*-value) therefore we used a separate model disaggregated by gender. There were no males in the youngest category therefore only females are shown in the table.
 †Significant at the 0.05 level.

a recently infected study participant: “The way he was expressing himself it is like he went to confront the lady”. Another reported that a participant refused recency testing because he was afraid he “might kill the person who infected [him].” When asked about participant perspectives regarding recent infection testing, health care providers gave mixed responses. Perception of negative participant perspective included disinterest, risk of retraumatization, and fear of interpersonal conflict.

DISCUSSION

We found that 8.6% of persons newly diagnosed with HIV infection at EDARP sites had been recently infected. Young women had the highest proportion of new infections. This may be related to the gender differences in care-seeking.^{16,17} Work-related mobility, clinic hours, and gender norms often discourage men from seeking health care early.^{18,19} Differential health-seeking behavior affects the use of recent infection data to estimate incidence and in tracking the epidemic.

Our study corroborated that partner notification services are very effective in increasing yield in routine HIV testing; however, our sample was too small to say whether index clients with recent infection are more likely to refer partners with recent infection. What is apparent is that recent infections identified more persons who were unaware of their serostatus.

Interviews with health care providers revealed unexpected clinical benefits associated with recent infection testing. Clients seemed to view recent infection status and

VL measurement as indicators of disease progression; those with confirmed recent infections or low VL were hopeful for favorable health outcomes, which encouraged adherence. A full evaluation needs to be done to understand whether recency infection testing increases the risk of psychosocial harm or intimate partner violence beyond the risks associated with HIV status disclosure.

Our study had limitations. Our sample was small and, moreover, unlikely representative of all HIV-infected people living in the EDARP catchment area. We are therefore unable to make broad generalizations or to calculate incidence accurately.

CONCLUSIONS

We found that integrating recent infection testing into routine HTC services in Kenya is feasible and acceptable. More data are needed to understand issues related to return of results and how best to use individual and population data on recent infection.

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