Research Letter

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Extremely low hepatitis C prevalence among HIV co-infected individuals in four countries in sub-Saharan Africa

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A multicentric, retrospective case-series analysis (facility-based) in five sites across Kenya, Malawi, Mozambique, and Uganda screened HIV-positive adults for hepatitis C virus (HCV) antibodies using Oraquick rapid testing and viral confirmation (in three sites). The results reveal a substantially lower prevalence than previously reported for these countries, suggesting that targeted integration of HCV screening in African HIV programs may be more impactful than routine screening.

Prior research on hepatitis C virus (HCV) infection in sub-Saharan Africa is limited and methodologically inconsistent, often characterized by poor categorization of individuals from high-risk groups, lack of virological confirmation of active disease, and bias from environmental factors (e.g. reduced case detection specificity from Schistosoma*)* [1–4]. Furthermore, reported HCV co-infection prevalence is highly variable in Africa, ranging from 3.3% in southern regions to 42.3% in the north.

We conducted a retrospective case-series analysis in health facilities and hospitals in five African countries with varied HIV prevalence settings, the largest observational analysis of HIV/HCV co-infection in Africa to date.

Patients were selected from five Médecins Sans Frontières facilities in four countries with varying HIV prevalence: Mbarara, Uganda (7.9% adult HIV prevalence); Maputo, Mozambique (16.9%); Chiradzulu, Malawi (17.0%), Kibera, Kenya (an impoverished quarter of Nairobi) (12.6%), and rural Homa Bay County, Kenya (27.1%) [5–9]. Patients were eligible if they were at least 18 years old, infected with HIV, and screened for HCV between January 2014 and December 2016. HIV patients with long-term antiretroviral therapy (ART) exposure and with uncomplicated, advanced stages of HIV disease were included. People-who-use-drugs (PWUD) were included at one site (Mozambique).

HCV screening procedures were similar across sites. HCV care was integrated into routine care for HIV differently depending on the site: during patients' initial diagnosis or during follow-up counseling sessions (Uganda) or upon initiation of ART care or during annual HIV viral load testing (Kenya: Kibera). At two sites, HCV screening was already integrated into preexisting procedures for observational studies exploring the disease of long-term ART recipients (Malawi) and hospitalized inpatients (Kenya: Homa Bay) [10]. For each site, procedures were adapted for the local context and according to national policies, conducted in collaboration with the National Ministry of Health.

Preliminary serological screening of whole blood samples was conducted at all sites using the OraQuick HCV rapid qualitative test (OraSure Technologies, Bethlehem, Pennsylvania, USA), a WHO prequalified immunoglobulin G HCV antibody immunoassay [sensitivity = 100% (95% CI: 97.8–100.0), specificity = 99.4% (95% CI: 97.3–99.8)] [11]. Antibody-positive patients were further confirmed for replicative infection using two different real-time PCR (RT-PCR) viral load measures: PCR Roche COBASAmpliprep/COBASTaqMan (Mozambique and Uganda) and Abbott m2000 (Kenya: Kibera). Patients with confirmed active infection received baseline clinical assessments and viral genotyping from accredited laboratories using either dried blood spot cards (Uganda) or frozen plasma (Kenya and Mozambique). Upon confirmation of a positive result, all patients were offered standard treatment with Direct Acting Antivirals (DAA).

Study databases used RedCap v.5.7.3 software (Vanderbilt University, Nashville, Tennesee, USA) in Malawi, Kenya: Homa Bay, and Mozambique; EpiData v.3.1 (Odense, Denmark) in Uganda; and Microsoft Excel in Kenya: Kibera. Analysis occurred in STATA v.13 (College Station, Texas, USA). Upper and lower confidence bounds were calculated using an open source sample size calculator (University of California, San Fransisco, California, USA) [12]. All studies were Ethics Review Boards-approved, sought consent, and applied data protection practices for participants.

In total, 15 336 HIV patients were screened for HCV antibodies, and 0.4% tested positive (Table 1). HCV antibody prevalence among those screened was higher in Mozambique (30/2600; 1.15%, 95% CI: 0.81–1.64) compared with Malawi (2/385; 0.5%, 95% CI: 0.14–1.87), Uganda (18/7500, 0.24%, 95% CI: 0.15–0.38), and Kenya (Kibera: 10/4500; 0.22%, 95% CI: 0.12–0.41; Homa Bay: 1/351; 0.28%, 95% CI: 0.05–1.59). In

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Table 1. Hepatitis C virus screening results among HIV patients and characteristics of virologically confirmed chronic hepatitis C patients in five sub-Saharan sites, 2014–2016.

						Confirmed CHC patients				
Sites	Population	Screened patients	Reactive HCV RDT positive serology *N* [% (95% CI)]	Detectable HCV VL/tested	Confirmed CHC/total screened percent	Median age (year)	% female	Genotype *n/N* (%)	Median viral load (IU/ml)	Treatment
Mozambique	Advanced HIV or PWUD	2600	30 (1.15% [0.81–1.64])	26/30 (86%)	1.0% (0.68–1.46)	40	0/26 (0%)	GT1 13/16 (81%) GT3 1/16 (6%) GT4 2/16 (13%)	769 000	Sof + Dac
Kenya: Kibera	HIV+	4500	10 (0.22% [0.12–0.41])	2/10 (20%)	0.04% (0.01–0.17)	36	1/2 (50%)	GT4 2/2 (100%)	3 014 583	Sof + Led
Uganda	HIV+	7500	18 (0.25% [0.15–0.38])	5/17 (29%)	0.07% (0.03–0.16)	43	5/5 (100%)	GT4 5/5 (100%)	2 990 000	Sof + Led
Malawi	HIV+ on ART ≥10 years	365	2 (0.52% [0.14%-1.87%])	N/A	N/A	XX	–	–	–	–
Kenya: Homa Bay	HIV+ inpatients	351	1 (0.28% [0.05–1.59])	N/A	N/A	XX	–	–	–	–
Total	–	15 316	61 (0.3%)[a]	33/57 (57.9%)		–	6/33	–	–	–

*In Uganda, one patient was lost to follow-up between their serological test and viral confirmation. CHC, chronic hepatitis C; Dac, Daclatasvir; GT, genotype; Led, ledipasvir; PWUD, people who use drugs; RDT, rapid diagnostic test; Sof, sofosbuvir.
[a]Aggregated analysis only, not a pooled/weighted figure.

Mozambique, many patients were PWUD; among the screened PWUD, 79% presented HCV-positive antibody.

Active HCV infection confirmed by HCV viral replication (Kenya: Kibera; Mozambique; Uganda), was low: 0.04% ($n = 2/4500$; 0.01–0.17), 1% ($n = 26/2600$; 95% CI: 0.68–1.46), and 0.07% ($n = 5/7500$; 0.03–0.16). Characteristics of individuals with confirmed replicative viral HCV infection (e.g. genotype, viral load, treatment, and demographics) are shown in Table 1.

HCV-antibody and PCR-positivity prevalence measured in our study were substantially lower than pooled estimates from other studies conducted in the same five countries [1], neighboring African countries, and other low-resource contexts [13–15]. This may be explained by a number of differences unique to our study: patient characteristics (e.g. exclusively HIV-infected patients, PWUD); differences in screening strategies; or variation in the performance of serological rapid diagnostic tests (e.g. Oraquick was the only WHO-prequalified rapid diagnostic test (RDT) at the time of study, it has not been widely tested in field situations in African settings or in HIV-infected populations [16,17]).

There was some variation between our sample sites. The Mozambican PWUD sub-group observed the highest levels of antibody-prevalence and viral confirmation, confirming that even when prevalence is low, PWUD are especially susceptible to HCV infection and may require targeted screening. In Uganda, viral genotyping revealed exclusively Type 4 HCV, diverging from previous evidence finding only Type 1 in the country [1,18]. Linked with choice of regimen, the difference is important, whereas research on this issue is evolving and few data are available overall. In addition, sex differences between sites (high proportion of women in Ugandan HCV-confirmed patients, high proportion of men in Mozambican HCV-confirmed patients) were likely because of gendered risk behaviors, such as injection drug use.

There were some limitations in this study. Except for the Mozambican PWUD, these patients may not have had HCV risk factors. Database limitations prevented analysis of a potential cohort effect when individuals had already died. Information on co-infection with HCV and Schistosomiasis was unavailable, though prior literature has suggested causes of a high HCV false positivity screening percentage in these moderate-to-high Schistosoma-prevalent countries. Statistical variance ('false-positive paradox') may have led to more false-positive results compared with true positives when low incidence rates were lower than false-positive rates [3,19,20].

In summary, our results not only demonstrate the feasibility of large-scale HCV screening during HIV care using simplified rapid testing, but also confirm that HCV does not seem to be the public health burden in the sites investigated that it is in other regions, particularly among people living with HIV. Future HCV screening strategies in the region should consider these findings when determining policy (MSF has already replaced systematic HCV screening for HIV-positive patients at study sites with a risk factor and symptomatic screening algorithm, prioritizing PWUD). Policy changes will be more efficient if they also increase access to testing and treatment.

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Conflicts of interest

There are no conflicts of interests.

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