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Hepatitis C Knowledge and Recent Diagnosis Affect Hepatitis C Treatment Willingness in Persons Living With HIV

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Background: We assessed the impact of health literacy and hepatitis C (HCV) knowledge on HCV treatment willingness among people living with HIV (PLWH) at an academic HIV clinic.

Methods: Cross-sectional analysis of PLWH coinfected with HCV who completed health literacy, HIV literacy, and HCV knowledge inventories. We estimated the prevalence of low health literacy, HIV knowledge, and HCV knowledge sampled from 3-comparison groups: PLWH not referred for HCV, referred but who "not showed" to the HCV clinic, and referred and attended the HCV clinic. We used mixed-model linear and logistic regression to ascertain predictors of low health literacy, HIV knowledge, HCV knowledge, and predictors of willingness to start HCV treatment.

Results: We enrolled 151 PLWH; 17% were female, 38% non-White, and 60% without a high-school education. Approximately, 68% were men who have sex with men, of whom 62% used intravenous drugs. The prevalence of low health, HIV knowledge, and HCV knowledge was 10%, 32%, and 29%, respectively. Predictors of low health literacy were being Hispanic, cirrhotic, and not completing high-school education. Low HCV knowledge was observed in female, non-White, and those diagnosed with HCV for a decade. In adjusted analyses, PLWH living with HCV for a decade (OR: 0.23) were less likely to be very willing to be treated for HCV. By contrast, those with high HCV knowledge were more likely to be very willing to receive treatment (OR: 1.27).

Conclusion: Low HCV knowledge and living with HCV for at least a decade are under-recognized negative predictors for PLWH's willingness to receive HCV treatment.

Clinical Trials Registration: ClinicaTrials.gov identifier: NCT20170991.

Key Words: health literacy, HCV knowledge, HIV literacy, treatment willingness, and HIV

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INTRODUCTION

As of 2020, the United States is among many advanced countries missing targets for hepatitis C (HCV) elimination.[1] HCV treatment is the last step in the HCV cascade of screening, diagnosis confirmation, linkage, and care.[2]

Health literacy is defined as "the degree to which individuals can obtain, process, understand, and communicate about health-related information needed to make informed health decisions." 3 Health literacy is often an overlooked factor influencing engagement in care and health outcomes.[4,5] Low health literacy has been linked to poor medication adherence, lower CD4 cell counts, higher HIV viral loads, and more frequent hospitalizations among people living with HIV (PLWH).[6,7] HCV knowledge generally includes understanding different domains, including the natural history of HCV disease, current HCV therapies, and post-HCV therapy benefits and limitations, including a lack of subsequent reinfection protection.[8] A few studies have described HCV knowledge in patients with ongoing substance use,[9] but little is known about PLWH knowledge of their HCV disease process.

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Edward Cachay: study concept and design, analysis and interpretation of data, drafting of the article, critical revision of the article, obtained funding, study supervision, and approved the final submission. Francesca Torriani: patient recruitment, critical revision of the article, and approved the final submission. Lucas Hill: patient recruitment, critical revision of the article, and approved the final submission. Amutha Rajagopal: patient recruitment, critical revision of the article, and approved the final submission. Jeffrey Yin: patient recruitment, critical revision of the article, and approved the final submission. Laura Bamford: critical revision of the study design, article, and approved the final submission. Wm. Christopher Mathews: direct contribution to study design, statistical analysis, and interpretation of data, critical revision of the article, and approved the final submission.

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Most PWLH under care are screened for HCV and know their serostatus,[10] but effective linkage to HCV care remains suboptimal.[11] Indeed, "no-show" rates in our HCV coinfection clinic have doubled since direct-acting antivirals (DAAs) licensing despite more unrestricted access to HCV treatment with better outcomes.[12] Multiple factors influence medical providers' decision to refer PLWH for HCV treatment. Ongoing alcohol or substance use, psychiatric illness, and unstable housing limit the ability of PLWH to follow steps required to treat their HCV.[13] It is unknown how HCV knowledge or health literacy influence PLWH's willingness to be treated. We hypothesized that the prevalence of low health literacy and HCV knowledge among PLWH coinfected with HCV is high. Furthermore, we hypothesized that low HCV knowledge and health literacy influence their willingness to seek HCV treatment, indirectly influencing HCV treatment "no-show" rates. Therefore, we conducted this study to ascertain and compare the levels of HCV knowledge, health literacy, and their effect on HCV treatment willingness among PLWH coinfected with HCV as sampled from 3 groups defined by the HCV referral status: (1) those not referred for HCV therapy, (2) those referred but "not showed" to the HCV clinic, and (3) those referred and who attended HCV clinic in a large academic HIV clinic in the United States.

METHODS

Study Design and Population

This cross-sectional survey prospectively enrolled adult (≥18 years) PLWH with active HCV infection, defined as having a detectable HCV viral load. All eligible participants attending an HIV primary care appointment at the University of California, San Diego (UCSD) Owen Clinic between October 2017 and July 2020 completed structured health literacy, HIV knowledge, and HCV knowledge assessments. Our standard of care requires that a HIV primary care medical provider promptly refers PLWH with active HCV infection to the Owen Hepatitis Co-Infection Clinic, a once weekly subspecialty clinic colocated within the main HIV primary care clinic.[14] It is up to the HIV medical provider's clinical discretion to decide the best timing for HCV treatment referral after a routine HIV medical appointment. At the time of study enrollment, we assigned each study participant to either being referred or not to our HCV clinic based on medical provider disposition. We followed all eligible enrolled participants up to 3 months after the last patient enrolled to allow the last study participants enough time to attend our HCV clinic. The follow-up allowed proper patient reassignment to the HCV referral group if they were referred to HCV in a subsequent HIV primary care visit after study enrollment. Hence, resulting in 1 of 3 groups at the end of the study (1) PLWH nonreferred for HCV, (2) those referred but "not showed" to the HCV clinic, and (3) those referred and attended the HCV clinic. Exclusion criteria included having a neurocognitive impairment precluding participation, physical illness limiting assessment, and prior HCV therapy. All participants signed written consent before study enrollment. The study protocol was approved by the UCSD Institutional Human Research Protection Program and registered in clinical trials.gov (# 20170991).

Study Measurement Instruments

We used the validated short-form Test of Functional Health Literacy in Adults (s-TOFHLA) to assess general health literacy.[15] The s-TOFHLA raw scores can range from 0 to 36 and are categorized as inadequate 0–16, marginal 17–22, or adequate health literacy 23–36. To ascertain HIV knowledge, we used the Brief Estimate of Health Knowledge and Action—HIV version scale (BEHKA-HIV).[16] The BEHKA-HIV consists of an 8-item scale, and HIV-health literacy scores range from 0 to 8: inadequate 0–3, marginal 4–5, and adequate 6–8. For assessment of hepatitis C knowledge, we used a modified version of the scale for HCV knowledge developed by the National Center in HIV Social Research of the University of New South Wales, Australia.[17] In the DAA era, the specific items requiring modification pertain to therapy duration, chances of HCV cure, and side effects. The modified HCV knowledge scale scores range from 0 to 12, and responses are categorized as inadequate 0–3, marginal 4–7, and adequate HCV knowledge 8–12. We defined low health literacy, HIV knowledge, and HCV knowledge as having either inadequate or marginal scores. The assessment of willingness and urgency for HCV treatment consisted of 2 items, each using a 5-point Likert-type scale. The first measures willingness to undertake treatment (a score of 1 indicating very willing and 5 indicating not willing at all). The second measures the time frame when patients plan to undertake HCV treatment (within 1 year to never). All instruments were available in English and Spanish (see supplementary information for the description of each assessment inventory).

Data Collected Domains and Study Definitions

Electronic medical record (EMR)-extracted data included patient demographics, education level, HIV and HCV transmission risk factors, CD4 cell count, and HIV viral load. We collected information on HCV genotype, HCV viral load, cirrhosis status, and comorbidity burden (measured by the Charlson comorbidity score).[18] Cirrhosis diagnosis was based on standard clinical criteria using either liver elastography or liver biopsy results or ICD-10 codes of cirrhosis or ESLD diagnosis. For time-varying covariates, the value collected was the one most immediately before, but no longer than 3 months before the assessment date.

For screening of ongoing self-reported substance use, depression, and alcohol use disorder within the last 3 months of assessments, patients completed the National Institute on Drug Abuse—Alcohol, Smoking, and Substance Involvement Screening Test (NIDA-ASSIST),[19] the PHQ-9 inventory,[20] and the Alcohol Use Disorders Identification Test (AUDIT-C) instruments,[21] respectively. We also conducted EMR review to assess physician documentation of a history of psychiatric hospitalization or active psychiatric-related symptoms, risk behaviors, drug type, and consumption frequency. The housing status was collected through diagnosis code abstraction of homelessness, lack of housing, or EMR documentation of frequent short stays (up to 2-weeks) in motels or different friends or family members' residences.

TABLE 1. Health Literacy, HCV Knowledge, HIV Health Literacy and Demographics, HIV, HCV, and Participants Characteristics According to the HCV Treatment Referral Group

Factor	Overall Cohort	Referral Status			*P*
		Not Referred	Referred But Not Showed	Referred and Attended	
N	151	51	22	78	
S-TOFHLA score median (IQR)	35 (32, 35)	35 (34, 35)	34 (32, 35)	35 (32, 36)	0.32*
S-TOFHLA level					
Inadequate	10 (6.6%)	4 (8%)	1 (5%)	5 (6%)	0.88†
Marginal	5 (3.3%)	1 (2%)	0 (0%)	4 (5%)	
Adequate	136 (90.1%)	46 (90%)	21 (95%)	69 (88%)	
HCV knowledge score, median (IQR)	9 (7, 10)	8 (7, 9)	8 (6, 9)	9 (7, 10)	0.27*
HCV knowledge level					
Inadequate	2 (1.3%)	1 (2%)	0 (0%)	1 (1%)	0.48†
Marginal	46 (30.5%)	13 (25%)	10 (45%)	23 (29%)	
High	103 (68.2%)	37 (73%)	12 (55%)	54 (69%)	
HIV knowledge, BEHKA score, median (IQR)	7 (5, 8)	6 (5, 8)	6 (5, 7)	7 (6, 8)	**0.015***
HIV knowledge, BEHKA level					
Inadequate	10 (6.6%)	5 (10%)	2 (9%)	3 (4%)	**0.013**†
Marginal	33 (21.9%)	17 (33%)	6 (27%)	10 (13%)	
Adequate	108 (71.5%)	29 (57%)	14 (64%)	65 (83%)	
Willingness for HCV Rx					
Very willing	127 (84.1%)	41 (80%)	16 (73%)	70 (90%)	0.13†
Somewhat willing	8 (5.3%)	3 (6%)	3 (14%)	2 (3%)	
Unsure	12 (7.9%)	6 (12%)	2 (9%)	4 (5%)	
Somewhat unwilling	1 (0.7%)	0 (0%)	1 (5%)	0 (0%)	
Not at all willing	3 (2.0%)	1 (2%)	0 (0%)	2 (3%)	
Willing time					
Within 1 yr	143 (94.7%)	49 (96%)	20 (91%)	74 (95%)	0.30†
Within 2 yrs	4 (2.6%)	0 (0%)	1 (5%)	3 (4%)	
Within 2–5 yrs	2 (1.3%)	1 (2%)	0 (0%)	1 (1%)	
Never	2 (1.3%)	1 (2%)	1 (5%)	0 (0%)	
Age, median (IQR)		48 (39, 52)	45.5 (36, 53)	50.5 (41, 57)	0.06*
Age (quartiles)					
20	28 (18.5%)	9 (18%)	6 (27%)	13 (17%)	**0.044**†
37	47 (31.1%)	19 (37%)	8 (36%)	20 (26%)	
49	34 (22.5%)	15 (29%)	5 (23%)	14 (18%)	
55	42 (27.8%)	8 (16%)	3 (14%)	31 (40%)	
Birth sex					
Female	26 (17.2%)	15 (29%)	2 (9%)	9 (12%)	**0.024**†
Male	125 (82.8%)	36 (71%)	20 (91%)	69 (88%)	
Race					
White	94 (62.3%)	32 (63%)	13 (59%)	49 (63%)	0.32†
Black	16 (10.6%)	5 (10%)	0 (0%)	11 (14%)	
American Indian	1 (0.7%)	0 (0%)	1 (5%)	0 (0%)	
Asian	4 (2.6%)	2 (4%)	1 (5%)	1 (1%)	
Mixed race	34 (22.5%)	11 (22%)	7 (32%)	16 (21%)	
Others	2 (1.3%)	1 (2%)	0 (0%)	1 (1%)	
Race: non-White					
White	94 (62.3%)	32 (63%)	13 (59%)	49 (63%)	0.95†
Non-White	57 (37.7%)	19 (37%)	9 (41%)	29 (37%)	
Ethnicity					1.00†
Non-Hispanic	109 (72.2%)	37 (73%)	16 (73%)	56 (72%)	
Hispanic	42 (27.8%)	14 (27%)	6 (27%)	22 (28%)	

(*continued on next page*)

TABLE 1. (*Continued*) Health Literacy, HCV Knowledge, HIV Health Literacy and Demographics, HIV, HCV, and Participants Characteristics According to the HCV Treatment Referral Group

Factor	Overall Cohort	Referral Status			*P*
		Not Referred	Referred But Not Showed	Referred and Attended	
Education level					
≤High school	62 (41.1%)	22 (43%)	12 (55%)	28 (36%)	0.41†
>High school	60 (39.7%)	22 (43%)	7 (32%)	31 (40%)	
Missing	29 (19.2%)	7 (14%)	3 (14%)	19 (24%)	
HIV transmission risk					
MSM	42 (27.8%)	12 (24%)	3 (14%)	27 (35%)	**0.049**†
Heterosexual	11 (7.3%)	3 (6%)	3 (14%)	5 (6%)	
Hemophilia	1 (0.7%)	0 (0%)	0 (0%)	1 (1%)	
MSM + IDU	61 (40.4%)	17 (33%)	10 (45%)	34 (44%)	
Heterosexual + IDU	35 (23.2%)	19 (37%)	6 (27%)	10 (13%)	
Others	1 (0.7%)	0 (0%)	0 (0%)	1 (1%)	
Years known living with HIV, median (IQR)	14 (6, 21)	14 (6, 22)	11.5 (4, 16)	14 (7, 22)	0.42*
CD4 (most recent), median (IQR)	503 (271, 718)	476 (250, 637)	648 (427, 781)	513 (271, 714)	0.27*
CD4 stratum					
≤200	24 (15.9%)	10 (20%)	1 (5%)	13 (17%)	0.69†
201–350	27 (17.9%)	10 (20%)	4 (18%)	13 (17%)	
351–500	24 (15.9%)	9 (18%)	3 (14%)	12 (15%)	
≥501	76 (50.3%)	22 (43%)	14 (64%)	40 (51%)	
HIV pVL, median (IQR)	26 (0, 743)	87 (0, 6820)	10.5 (0, 262)	0 (0, 112)	**0.020***
HIV viral load					
Undetectable	69 (46.0%)	15 (29%)	11 (50%)	43 (56%)	**0.011**†
Detectable	81 (54.0%)	36 (71%)	11 (50%)	34 (44%)	
Prior OI					
No	122 (80.8%)	41 (80%)	17 (77%)	64 (82%)	0.85†
Yes	29 (19.2%)	10 (20%)	5 (23%)	14 (18%)	
Known years with HCV, median (IQR)	5 (1, 10)	5 (1, 10)	5.5 (2, 8)	3.5 (1, 11)	0.83*
HCV risk factor					
MSM	41 (27.2%)	11 (22%)	3 (14%)	27 (35%)	0.061†
Heterosexual	10 (6.6%)	3 (6%)	3 (14%)	4 (5%)	
Hemophilia	1 (0.7%)	0 (0%)	0 (0%)	1 (1%)	
MSM + IDU	62 (41.1%)	18 (35%)	10 (45%)	34 (44%)	
Heterosexual +IDU	36 (23.8%)	19 (37%)	6 (27%)	11 (14%)	
Other	1 (0.7%)	0 (0%)	0 (0%)	1 (1%)	
HCV genotype					
1	118 (78.1%)	34 (67%)	17 (77%)	67 (86%)	**0.011**†
2	11 (7.3%)	4 (8%)	0 (0%)	7 (9%)	
3	17 (11.3%)	9 (18%)	4 (18%)	4 (5%)	
4	2 (1.3%)	1 (2%)	1 (5%)	0 (0%)	
Unknown	3 (2.0%)	3 (6%)	0 (0%)	0 (0%)	
log10(HCV pVL), median (IQR)	6.35 (5.7, 6.82)	6.31 (5.47, 6.75)	6.34 (5.9, 6.67)	6.4 (5.8, 6.94)	0.33*
Liver fibrosis					
F0	10 (6.6%)	2 (4%)	3 (14%)	5 (6%)	0.37†
F1	67 (44.4%)	20 (39%)	8 (36%)	39 (50%)	
F2	33 (21.9%)	14 (27%)	7 (32%)	12 (15%)	
F3	11 (7.3%)	3 (6%)	2 (9%)	6 (8%)	
F4	26 (17.2%)	9 (18%)	2 (9%)	15 (19%)	
Unknown	4 (2.6%)	3 (6%)	0 (0%)	1 (1%)	
Cirrhosis					
No	124 (82.1%)	41 (80%)	20 (91%)	63 (81%)	0.56†
Yes	27 (17.9%)	10 (20%)	2 (9%)	15 (19%)	
Alcohol use					
No	93 (61.6%)	38 (75%)	11 (50%)	44 (56%)	**0.053**†
Yes	58 (38.4%)	13 (25%)	11 (50%)	34 (44%)	

TABLE 1. (*Continued*) Health Literacy, HCV Knowledge, HIV Health Literacy and Demographics, HIV, HCV, and Participants Characteristics According to the HCV Treatment Referral Group

Factor	Overall Cohort	Referral Status			*P*
		Not Referred	Referred But Not Showed	Referred and Attended	
Drug use					
No	68 (45.0%)	27 (53%)	6 (27%)	35 (45%)	0.13†
Yes	83 (55.0%)	24 (47%)	16 (73%)	43 (55%)	
Psychiatric disease					
No	62 (41.1%)	18 (35%)	10 (45%)	34 (44%)	0.57†
Yes	89 (58.9%)	33 (65%)	12 (55%)	44 (56%)	
Unstable housing					
No	106 (70.2%)	33 (65%)	13 (59%)	60 (77%)	0.15†
Yes	45 (29.8%)	18 (35%)	9 (41%)	18 (23%)	
Charlson comorbity median (IQR)	2 (1, 5)	2 (1, 4)	2 (1, 3)	3 (1, 6)	0.68*

*Kruskal–Wallis test.
†Fisher exact.
IQR, interquartile range; MSM, men who sex with men; OI, prior opportunistic infection; pVL, plasma viral load; Rx, Treatment.

Statistical Plan

Using the validated cut-off points for each administered instrument, we calculated the point prevalence of low health literacy, HIV knowledge, and HCV knowledge in the overall cohort and then according to each of our 3-comparison groups: (1) PLWH nonreferred for HCV, (2) those referred but "not showed" to the HCV clinic, and (3) those referred and attended the HCV clinic. We used the Fisher exact test to compare the proportions of PLWH referred for HCV clinical attendance according to our 3 groups. Then, we used mixed-model regression to ascertain predictors of low health literacy, HIV knowledge, and HCV knowledge. Model covariates included sociodemographics, HIV characteristics, liver, and HCV-related features, Charlson comorbidity score, ongoing alcohol (AUDIT-C score $\geq$ 4), drug use (NIDA-ASSIST score $\geq$ 27), psychiatric disease, and unstable housing. The sociodemographic domain included age, sex, race/ethnicity, and level of education. The HIV-related domain included HIV transmission risk factor, CD4 cell count strata, HIV viral load, and time since HIV diagnosis. Liver and HCV-related factors included HCV genotype, viral load, cirrhosis status, and time since HCV diagnosis. Model estimates are presented as coefficients with corresponding standard errors with 95% confidence intervals (CI). Finally, we assessed predictors of unwillingness to initiate HCV treatment using logistic regression models. We dichotomized our dependent variable as "very willing" vs. "somewhat willing or less." Regression models accounted for the hierarchical nesting of patients within the referral group. Variables significant ($P < 0.10$) in bivariate models were examined as independent predictors of willingness to start HCV therapy in the overall cohort. We conducted an internal validation of the binary measure of HCV willingness by examining the relationship between treatment willingness and outcome of referral among those referred for HCV treatment. We hypothesized that those more willing to receive treatment would be more likely to attend a scheduled appointment than those less willing. We also performed a most discriminating cut point analysis using the original Likert scaled willingness variable. We estimated the receiver operating characteristics (ROC) area to predict HCV visit attendance given referral. Statistical analysis was conducted using Stata Version 16.1.

RESULTS

During the study period, we approached 154 PLWH. Three refused participation because of acute medical conditions, leaving 151 PLWH who were enrolled. Participants had a median of 16 years since being diagnosed with HIV and 5 years since HCV diagnosis. Their median age was 49 years, 17% were female, 38% non-White, and 60% did not complete high school. Fifty-four percent had detectable HIV viremia. HCV risk factors included men who had sex with men (68%), of whom 62% had either a history of or reported current injection drug use (IDU). HCV genotype 1 was the most frequent (78%), and 18% of participants had cirrhosis. Ongoing hazardous alcohol use, substance use, unstable housing, and mental illness prevalence was 38%, 55%, 30%, and 59%, respectively. The median Charlson comorbidity score was 2 among participants. Of the 151 PLWH assessed, 66% (100 patients) were referred for HCV treatment. Among those referred, 22% failed to attend their HCV clinic appointment (Table 1).

Overall, the prevalence of low health literacy, HCV knowledge, and HIV knowledge was 10%, 32%, and 29%, respectively. There was no difference in health literacy levels or HCV knowledge by the referral group. However, there was a significant difference in the prevalence of low HIV knowledge among those not referred (43%), referred but who "not showed" (36%), and referred and who attended HCV treatment (17%) ($P = 0.013$). Other factors noted to be associated with HCV nonreferral and lack of HCV attendance ($P < 0.05$) were being female, having uncontrolled HIV viremia, younger age, and heterosexual with IDU as a HIV risk factor, Table 1.

Independent predictors of low health literacy were being Hispanic, cirrhotic, and having less than high-school education. Low HCV knowledge was observed in female

TABLE 2. Mixed-Model Multiple Regression Predictors of Low Health Literacy, HCV Knowledge, and HIV knowledge*

	Predictors of Low Health Literacy			
	Coefficient	**Std Err**	**95% CI**	***P***
Age				
37	−0.77	1.275	−3.274 to 1.725	0.544
49	−2.659	1.465	−5.531 to 0.213	0.070
55	−0.549	1.499	−3.486 to 2.389	0.714
Race	−1.935	1.041	−3.976 to 0.106	0.060
Ethnicity	−3.635	1.107	−5.804 to −1.466	**0.001**
Education level				
≥High school	2.049	0.974	0.140 to 3.958	0.035
Missing	−0.029	1.216	−2.412 to 2.354	0.981
HCV diagnosis time	-0.0953	0.0636	−0.220 to 0.030	0.134
Cirrhosis	−3.399	1.248	−5.845 to −0.953	**0.006**
Charlson comorbidity score	0.079	0.172	−0.259 to 0.416	0.647
Predictors of low HCV knowledge				
Sex	0.782	0.413	−0.028 to 1.592	0.058
Race	−0.955	0.317	−1.577 to −0.334	0.003
CD4 cell count	0.0008	0.0005	−0.0002 to 0.000171	0.105
HCV diagnosis time	−0.054	0.0202	−0.093 to −0.014	0.008
Predictors of low HIV knowledge				
Sex	−0.358	0.459	−1.258 to 0.542	0.435
Educational level				
≥High school	0.402	0.294	- 0.176 to 0.979	0.173
Missing	0.502	0.364	−0.212 to 1.215	0.168
HIV risk factor				
Heterosexual	−0.469	0.598	−1.642 to 0.704	0.433
Hemophilia	−1.079	1.543	−4.103 to 1.946	0.484
MSM + IDU	−0.385	0.311	−0.995 to 0.226	0.217
Heterosexual + IDU	−0.858	0.438	−1.717 to 0.0005	**0.050**
Others	0.544	1.515	2.425 to 3.513	0.719
CD4 count strata				
201–350	0.614	0.439	−0.247 to 1.474	0.162
351–500	1.372	0.455	0.480 to 2.264	**0.033**
≥501	0.923	0.378	0.182 to 1.665	**0.015**
HIV undetectable	−0.549	0.264	−1.066 to −0.032	**0.037**
HCV genotype (GT)				
GT 2	0.859	0.482	−0.085 to 1.804	0.074
GT 3	−0.209	0.439	−1.071 to 0.652	0.634
GT 4	0.942	1.109	−1.232 to 3.115	0.396
GT unknown	−0.070	0.908	−2.481 to 1.079	0.440
Psychiatric disease	−0.399	0.272	−0.931 to 0.133	0.142

IDU, intravenous drug use; MSM, men who have sex with men.
*Variables significant ($P < 0.10$) in bivariate models were examined as independent predictors of willingness to start HCV therapy in the overall cohort.

PWH, non-White, and those diagnosed with HCV for at least a decade. Being heterosexual and IDU, as their HIV risk factor, predicted having low HIV knowledge, whereas having an undetectable HIV viral load and CD4 cell count above 350 correlated with higher HIV knowledge scores, Table 2.

In unadjusted analysis, being very willing to receive HCV therapy was associated with knowing their HCV diagnosis 5 years or less, having adequate health literacy, HIV knowledge and HCV knowledge, and lower Charlson comorbidity scores (see Table 1, Supplement Digital Content, http://links.lww.com/QAI/B610). Persons older or with cirrhosis were less likely to be very willing to receive HCV treatment. In adjusted analyses, PLWH and with HCV for at least a decade (OR: 0.23) were less likely to be very willing to be treated for HCV. By contrast, those with high HCV knowledge were more likely to be very willing to receive treatment (OR: 1.27), Table 3. Our examination of the relationship between treatment willingness and outcome of referral among those referred for HCV treatment, conditional on being referred (n = 100), showed that the proportion not attending a scheduled HCV appointment was 18.6% among

TABLE 3. Mixed Effect Multiple Logistic Regression Predictors of Being "Very Willing" to Receive HCV Treatment*

	Predictors of Being Very Willing to Receive HCV Treatment			
	Odd Ratio	Std Err	95% CI	*P*
Health literacy level				
Adequate	1 (base)			
Inadequate or marginal	1.28	0.94	0.31 to 5.34	0.74
HCV knowledge score	1.27	0.16	1.00 to 1.63	**0.05**
HIV knowledge score	1.14	0.17	0 0.85 to 1.54	0.38
Age				
20	1 (base)			
37	0.42	0.49	0.04 to 4.13	0.46
49	0.25	0.30	0.03 to 2.58	0.24
55	0.31	0.39	0.03 to 3.47	0.34
HCV time from diagnosis (y)				
1	1 (base)			
5	0.72	0.54	0.16 to 3.13	0.66
10	0.23	0.15	0.07 to 0.81	**0.02**
Cirrhosis	0.57	0.35	0.17 to 1.88	0.36
Charlson comorbidity score	0.97	0.09	0.81 to 1.15	0.72

*Variables significant ($P < 0.10$) in bivariate models were examined as independent predictors of willingness to start HCV therapy in the overall cohort.

The level of significance was <0.05.

those very willing to be treated, while 42.9% among those less than very willing to be treated ($P = 0.042$). The corresponding odds ratio was 0.30 (95% C.I. 0.08–1.24). In a most discriminating cut point analysis using the original Likert scale willingness variable, the ROC area for prediction of visit attendance given referral was 0.59 (0.44 0.72). The most discriminating cut point was 1.5 (midway between very willing and willing).

Overall, HCV knowledge scores showed a moderate but significant correlation with both S-TOFHLA health literacy (Spearman rho = 0.23, $P = 0.005$) and BEHKA HIV knowledge scores (Spearman rho = 0.26, $P= 0.001$). The strongest correlation occurred between S-TOFHLA health literacy and BEKHA HIV knowledge scores (Spearman rho = 0.43, $P< 0.001$).

DISCUSSION

Facilitating linkage to HCV care has become a priority to achieve HCV elimination goals, yet, significant logistical challenges remain.[22] Cognizant that HIV and HCV are overlapping syndemic conditions,[23] we decided to concomitantly assess health literacy, HIV knowledge, and HCV knowledge at the time of routine clinical evaluation in an HIV primary care clinic caring for more than 3400 patients. The results here reported that approximately 1 in 10 PLWH coinfected with active HCV infection has low health literacy. About 1 in 3 has low HCV knowledge or HIV knowledge. PLWH, who had low HCV knowledge and knew their HCV diagnoses for longer than a decade, were less likely to be very willing to receive HCV therapy.

We noted that participants not referred or who missed their HCV appointments had lower HIV knowledge scores, were more often female, had uncontrolled HIV viremia, were young, and heterosexual with IDU. As we previously showed, different barriers mediate, directly or indirectly, providers' perceptions and patients' willingness to attend HCV care.[13] In this study, the prevalence of health care barriers, such as ongoing mental illness, alcohol, substance use, and unstable housing, was high. Similarly, patient characteristics commonly associated with marginal engagement in HIV care were also associated with HCV nonreferral. Still, this study adds to our understanding that those who either were not referred for HCV treatment or failed to establish HCV care had important gaps in HIV knowledge. Our findings call for increasing medical providers' awareness of the need to boost patient HIV knowledge to improve PLWH access and engagement in HIV and HCV care.

Our results revealed significant disparities. There were HCV knowledge gaps among PLWH of color, females, and older people despite many knowing their HCV diagnosis for a decade or longer. Low health literacy was prevalent among people of color who did not complete high school, perhaps contributing to difficulties navigating health systems that are not patient centered.[24,25] HCV is prevalent among PLWH with IDU, yet we observed that they have the highest proportion of low HIV knowledge scores and were the ones who more often failed to attend their HCV appointments after referral. Overall, our results showed that health literacy, HIV knowledge, and HCV knowledge are correlated and impact HCV therapy willingness. More importantly, they are critical psychosocial barriers that need to be addressed to facilitate HCV treatment and as others have shown HIV suppression, too, especially in PWLH with IDU and non-White communities.[26]

Low HCV knowledge identifies a group of PLWH who misperceive the mortality risk of untreated HCV and have increased concurrent personal barriers to care, negatively affects their willingness to receive HCV treatment. Different factors could influence the observation that PLWH with HCV diagnosis for a decade or longer have lower HCV knowledge levels. Some might have heard about HCV treatment during the interferon era but lack awareness of treatment advances in the DAA era. For others, the changes in access and coverage by payers for DAA might have created confused messaging from providers regarding their candidacy for HCV treatment and the impact of HCV on their health. Our data suggest that updating HCV knowledge through counseling of patients with long-standing diagnoses is paramount to facilitate HCV treatment access and uptake. Different models using peer navigators, case managers, and clinical pharmacists show promise[27–29] by linking patients with local resources, providing social support, and fostering problem-solving skills, finally, enabling them to connect to HCV care efficiently. This may be of value, particularly among PLWH females, people of color, IDU, and older populations.

Our study has limitations. We likely underestimated the prevalence of low health literacy as our studied PLWH were enrolled after attending a routine HIV clinical care appointment. Hence, our results cannot be generalized to PLWH

marginally or not engaged in care.[4] Our sample size was small (n =151) and, therefore, should be replicated in expanded coinfected cohorts. In addition, we recognize that the definition of health literacy is evolving; we used s-TOFHLA that aligns with the Institute of Medicine report "health literacy" and has been successfully used in various populations.[30] We used a previously published instrument to assess HCV knowledge, with modifications to reflect that DAA treatments are more efficacious, shorter, and better tolerated than interferon based. However, the modified HCV knowledge inventory used in this study has not been validated for use in PLWH. Finally, findings may not be generalizable to other geographical areas with different population demographics or health system access.[31] However, almost 40% of our participants were minorities similar to other inner-city HIV clinics in the United States.

In conclusion, low health literacy, HIV knowledge, and HCV knowledge are correlated and under-emphasized disincentives that impact HCV care among coinfected patients. Low HCV knowledge and living with HCV for a long time are overlooked factors for PLWH's willingness to receive HCV treatment.

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