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Hepatitis C Treatment Outcomes Among People Who Inject Drugs Accessing Harm Reduction Settings in Kenya

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ABSTRACT

Background: Data are limited on HCV treatment outcomes among people who inject drugs (PWID) in low- and middle-income countries (LMICs) and particularly sub-Saharan Africa.

Methods: We provided ledipasvir/sofosbuvir under directly observed therapy (DOT) to 95 PWID accessing medication-assisted treatment (MAT) and needle and syringe programs (NSP) in Nairobi and Coastal Kenya.

Results: Participants were predominantly male (n=81, 85.3%), mean age of 36.5 years (SD=±6.5); 38 (40%) were HIV-positive, 12 (12.6%) were cirrhotic, and 87 (91.6%) reported injecting drugs in the last 30 days. Genotypes were 53 (55.8%) 1a, 39 (41.1%) 4a, and 3 (3.2%) 1a/4a. Among 92 who initiated treatment, 85 (92.4%) completed treatment and 79 (85.9%) achieved SVR.

Conclusions: HCV treatment among PWID in an LMIC setting is feasible. Further research is necessary to ascertain optimal models of HCV care given NSP and MAT access is variable in LMICs, and DOT may not be sustainable with limited resources.

INTRODUCTION

Although between 10 and 15 million of the estimated 71 million people worldwide living with the hepatitis c virus (HCV), live in sub-Saharan Africa (SSA),[1] recent data suggest only 1% of these individuals have accessed HCV treatment.[1] Diminished access has been attributed to the financial and geographical barriers to general medical care, and limited regional availability of direct-acting antivirals (DAA). While wider availability to DAAs is anticipated, there are limited studies assessing HCV treatment outcomes for people in SSA, particularly for people who inject drugs (PWID). PWID are of particular importance due to an increased risk for HCV transmission. Given 22% of PWID in SSA are HCV antibody-positive – versus 52% of PWID globally[2,3] – earlier intervention could prevent the more widespread, established epidemics observed among PWID in higher income settings.

Given the limited data available from in low- and middle-income countries (LMICs), particularly in SSA, the goal of this study was to determine the effectiveness of introducing HCV treatment for PWID attending MAT and NSP sites in Kenya.

METHODS

Study population and recruitment

In this sub-study, a supplement to the Testing and Linkage to Care for Injection Drug Users (TLC-IDU) study (NCT01557998), we recruited 100 participants with chronic HCV from 9 NSP service sites in Nairobi and Coastal Kenya who were identified through the parent study.[4]

Prospective participants already received HCV antibody testing (SD Bioline, Standard Diagnostics, South Korea) and HCV RNA testing (Abbott Molecular, Des Plaines, IL, USA), and genotyped if viremic.[4] Eligible individuals were 18 years or older with chronic HCV identified from the parent study; living in Nairobi or Coast Province. Prospective participants confirming they were ready to start a three-month course of treatment, no upcoming plans to be mobile (e.g. trips, etc.), initiated treatment.

The study was approved by the Ethics and Research Committee of Kenyatta National Hospital (University of Nairobi) and the Yale University Institutional Review Board. All participants provided written informed consent.

Procedures

Once enrolled, all participants received a clinical evaluation including a physical examination, laboratory review, and counseling regarding HCV and DAA therapy. Participants were counseled on the side effects of DAAs, importance of adherence, liver health, and risk for HCV reinfection. Physical exams included vital signs, weight (to assess creatinine clearance), and a full multisystem exam with a focus on the liver. HIV and hepatitis B virus (HBV) tests (HIV-1/2 3.0 and HBsAg, SD Bioline, Standard Diagnostics, South Korea) were performed among all participants as well as a pregnancy test if female. Complete blood cell count, basic metabolic panel, and liver function tests were all assessed and Aspartate Aminotransferase to Platelet Ratio Index (APRI), fibrosis-4 (FIB-4), and Child-Turcotte-Pugh (CTP) scores were calculated.

All treatment-eligible and ready participants were offered fixed dose ledipasvir (LDV) 90 mg/sofosbuvir (SOF) 400mg via directly observed therapy (DOT) for an intended 12 weeks or 84 consecutive daily doses. Treatment was provided at 5 MAT sites – 2 in Nairobi, 3 in Coast (Malindi, Mombasa, Kwale), and 3 NSPs in Coast (Malindi, Mtwapa, Mombasa). For those on MAT, this required that participants visit their MAT program every day for treatment even if they accessed NSPs as well. Those only accessing NSPs were required to visit their NSP sites daily. If unable to come to the site, a peer case manager (PCM) brought the dose to the participant to ensure the dose was taken. In the event an individual missed a dose, their HCV treatment was extended a day for each dose missed. Participants were considered loss to follow-up if four weeks after a planned visit went by without contact and the participant's whereabouts were unknown to PCMs and the study team.

Treatment outcomes

Study visits occurred at treatment weeks 4, 8, and 12, and 12 weeks post-treatment. At each visit participants underwent a clinical evaluation and a pregnancy test if female, and HCV RNA testing using the Abbott RealTime HCV Assay (Abbott Molecular, Des Plaines, IL, USA). Sustained virologic response (SVR) was defined as having an HCV RNA level below 12 IU/mL at 12 weeks post-treatment completion. Individuals who had a detectable HCV viral load at post-treatment week 12 or those who were missing an HCV viral load at post-treatment week 12 were classified as a treatment failure.

RESULTS

Between July 2017 and April 2018, 100 participants were offered LDV/SOF through DOT. Of those offered, 95 accepted treatment and enrolled in this study. Participant demographic, clinical, and risk behavior data are presented in Table 1.

Participants were predominately male, 81 (85.3%) with mean age of 36.5 years (standard deviation, SD=±6.5). The majority of participants were from Mombasa (67.4%), followed by Malindi (18.9%) and Nairobi (13.8%). Most participants (91.6%) reported living in one place alone or with others and a similar proportion had an average monthly income of 10,000 KSH or higher, roughly $90 USD.

Of the 95 participants intended to receive HCV treatment, 69 (72.6%) were receiving MAT. All 95 participants were successfully genotyped; 53 (55.8%) were genotype 1a, 39 (41.1%) were genotype 4a, and 3 (3.2%) had mixed genotype 1a/4a. Among all participants, 38 (40%) were HIV-positive including four (4.2%) who were infected with HIV/HBV/HCV.

The majority 87 (91.6%) reported injection drug use in the last 30 days with an average of 3.1 (SD=±0.9) injections/day on the days they injected. The average age of first injection was 27.7 years (SD=±6.5). Among the 89 (93.7%) individuals who reported having ever being held in jail for at least 24 hours, incarceration occurred an average of 3.5 times over their lifetime. In the last year, 31 (32.6%) spent at least one night in jail/prison.

Regarding treatment outcomes among the 92 who initiated treatment, 85/92 (92.4%) participants completed treatment and 79/85 (92.9%) had a documented SVR (85.9% overall among those

initiated). Of the 16 participants who did not achieve SVR, one participant did not initiate treatment due to pregnancy prior to treatment initiation. Among the 13 participants who started treatment but did not achieve SVR, two were lost to follow-up early in the study, four discontinued treatment later on, three were missing SVR results (including one who died prior to the SVR collection), and four had a detectable viral load at week 12 post-treatment.

DISCUSSION

To our knowledge, this is the first study to evaluate HCV treatment outcomes among a cohort of PWID in the SSA, and one of the few assessing HCV treatment outcomes with DAA therapy among PWID in an LMIC. To date, studies examining HCV treatment outcomes among PWID using DAA therapy have been conducted predominantly in higher income settings.

While the overall rate of SVR among those initiated in our cohort (85.9%) is lower than that of other studies in SSA, most of the other studies did not solely enroll PWID. Of the 89% of participants achieving SVR in a cohort treated with LDV/SOF in Senegal, Côte d'Ivoire and Cameroon, participant baseline risk factors were not reported.[5] Similarly, individuals with active drug use were excluded from the Rwandan SHARED study where 98% of participants achieved SVR.[6] While lower than other cohorts in SSA, the rate of SVR among our participants is comparable to cohorts of PWID in other LMICs. PWID in an HCV treatment cohort in Myanmar achieved an overall SVR rate of 80%.[7] Similarly, 87% of a Bangladeshi HCV treatment cohort of PWID accessing harm services achieved SVR.[8] Furthermore, in an intent-to-treat analysis of

HCV treatment services for high risk groups in Ukraine, 78% of currently injecting PWIDs achieved SVR.[9]

To maximize treatment uptake and to mitigate barriers we co-located DAA therapy in MAT and NSPs under DOT and encouraged ongoing adherence with missed doses added to the end of treatment. In conjunction with the support from PCMs, most participants in this study were able to overcome barriers suggesting high rates of treatment completion and SVR can be achieved in SSA by co-locating HCV treatment in MAT and NSPs under DOT.

This study has some limitations. First, our participants were PWID recruited from NSP sites in Nairobi and Coastal Kenya who expressed interest in participating in this study among whom 95% accepted HCV treatment. Individuals utilizing these services may be more likely to seek HCV treatment and adhere to their medication compared to PWID who are not accessing these sites or engaged in research studies. Moreover, participants were treated using DOT. Therefore, our results may not be generalizable to PWID in LMICs where DOT is not used due to resource limitations.

In conclusion, as one of the first studies to assess HCV treatment outcomes for PWID in SSA and among the first to report on HCV treatment outcomes among PWID in the DAA era in an LMIC, our data suggest that providing HCV treatment in MAT and NSP sites is not only feasible but is also effective in achieving SVR in this population. Additional studies are necessary to assess optimal models of care for HCV treatment among PWID in LMICs, as DOT may not be a

feasible or cost-effective in all settings. Future studies will also need to evaluate reinfection following successful HCV treatment among PWID.

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Table 1: Demographic, risk factor, serological characteristics, and treatment outcomes among Kenyan PWID initiated on DAA therapy (n=95)	
Demographics	N (%), mean (± standard deviation) or median [IQR]
Age	36.5 (±6.5)
Gender	
Male	81 (85.3%)
Female	14 (14.7%)
Location	
Malindi	18 (18.9%)
Mombasa	64 (67.4%)
Nairobi	13 (13.7%)
Comorbidities	
HBV	5 (5.3%)
HIV	38 (40.0%)
On MAT	69 (72.6%)
Pregnant	1 (7.1%)
Relationship status	
Single	38 (40.0%)
Married	17 (17.9%)
Divorced or widowed	19 (20.0%)
Separated	16 (16.8%)
In a relationship but not living with partner	5 (5.3%)
Living situation	
In one place alone	21 (22.1%)
In one place with others	66 (69.5%)
Mobile	8 (8.4%)
Occupation	
Domestic service	2 (2.1%)
Skilled manual	7 (7.4%)
Unskilled manual	64 (67.4%)
Sales and services	15 (15.8%)
Other occupation	7 (7.4%)
Average monthly income	
Less than 10,000 KSH	8 (8.4%)
10,000+ KSH	87 (91.6%)
Virologic characteristics	
Genotype	
1a	53 (55.8%)
4a	39 (41.1%)
1a/4a	3 (3.2%)
Median APRI	0.5 [0.3-0.9]
Median FIB-4	1.1 [0.7-1.9]
Cirrhotic (FIB>= 3.25)	12 (12.6%)
History of injection drug use	
Ever injected drugs	95 (100.0%)
Average age of first injection	27.7 (±6.5)
Injected drugs in past 30 days	87 (91.6%)
Past 30 days how many times	85.1 (±37.6)

How many days in last month	26.8 (±9.1)
How many times on average day	3.1 (±0.9)
Criminal Justice History	
Ever held in jail for over 24 hours in lifetime	89 (93.7%)
Number of times held in jail in lifetime	3.5 (±2.8)
Last 12 months spend more than 1 night in jail	31 (32.6%)
Number of times held in jail in last 12 months	1.2 (±0.5)
Number of days in jail in past 12 months	85.1 (±86.9)
Treatment milestones (n=92)	
Completed treatment	85 (92.4%)
SVR	79 (85.9%)
Outcomes among those not achieving SVR (n=13)	
Early treatment discontinuation (took less than 14 doses)	2 (15.4%)
Mid-late treatment discontinuation (took between 14 and 84 doses)	4 (30.8%)
Detectable at post-treatment week 12 timepoint	4 (30.8%)
Missing post-treatment week 12 timepoint	3 (23.1%)
SVR by genotype	
1a (n=53)	44 (86.3%)
4a (n=39)	32 (84.2%)
mixed 1a/4a (n=3)	44 (86.3%)
APRI = AST to Platelet Ratio Index; Fib-4 = Fibrosis-4; MAT = medication-assisted treatment; NSP = needle and syringe programs; KSH = Kenyan Shilling, SVR = Sustained virologic response; SD = Standard Deviation; IQR = Interquartile range	