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Research Paper

Hepatitis C care continuum and associated barriers among people who inject drugs in Chennai, India[★]



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ABSTRACT

Background: Little is known regarding barriers to hepatitis C virus (HCV) treatment among people who inject drugs (PWID) in low-resource settings, particularly in the era of direct-acting antiviral therapies.

Methods: Between March, 2015–August, 2016, a cross-sectional survey was administered to community-based PWID in Chennai, India to examine the HCV care continuum and associated barriers. Adjusted prevalence ratios (APR) were estimated by multivariable Poisson regression with robust variance.

Results: All participants were male (n = 541); 152 participants had HCV mono-infection and 61 participants had HIV/HCV co-infection. Only one HCV mono-infected and one HIV/HCV co-infected participant was linked to HCV care. Overall, there was moderate knowledge of HCV disease but poor knowledge of HCV treatment. Higher total knowledge scores were negatively associated with HIV/HCV co-infection (vs. HCV mono-infection), though this was not statistically significant in adjusted analysis (APR = 0.71 [95%CI = 0.47–1.06]). Participants ≥ 45 years (APR = 0.73 [95%CI = 0.58–0.92]) and participants with HIV/HCV co-infection (APR = 0.64 [95%CI = 0.47–0.87]) were less willing to take weekly interferon injections for 12 weeks. Willingness to undergo HCV treatment improved with decreasing duration of therapy, higher perceived efficacy, and use of pills vs. interferon, though willingness to use interferon improved with decreasing duration of therapy. Most participants preferred daily visits to a clinic for HCV treatment versus receiving a month's supply. Participants ≥ 45 years (vs. < 45 years; APR = 0.70 [95%CI = 0.56–0.88]) and participants with HIV/HCV co-infection (APR = 0.75 [95%CI = 0.57–0.98]) were less likely to intend on seeking HCV care. Common reasons for not having already seen a provider for HCV treatment differed by HIV status, and included low perceived need for treatment (HCV-mono-infected), competing money/health priorities and costs/fears about treatment (HIV/HCV-reainfected).

Conclusion: Residual gaps in HCV knowledge and continuing negative perceptions related to interferon-based therapy highlight the need to scale-up educational initiatives. Readiness for HCV treatment was particularly low among HIV/HCV co-infected and older PWID, emphasizing the importance of tailored treatment strategies.

Introduction

Of the estimated 15.6 million people who inject drugs (PWID) worldwide, approximately 8.2 million have been infected with hepatitis C virus (HCV) (Degenhardt et al., 2017). Chronic HCV infection is a leading cause of cirrhosis, hepatocellular carcinoma, and premature

death (Cepeda et al., 2017; Greub et al., 2000; Kirk et al., 2013; Mehta et al., 2016). Prior to 2014, HCV treatment required weekly injections of pegylated interferon- α and daily doses of ribavirin for 24–48 weeks. These long-duration, interferon-based regimens were associated with suboptimal cure rates (\sim 50%) and severe side effects, leading to high rates of treatment discontinuation. However, with the advent of oral,

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pan-genotypic direct acting antivirals (DAAs), it is now possible to cure chronic HCV infection within 8–12 weeks in nearly all patients who have access to treatment (> 95% efficacy) (Falade-Nwulia et al., 2017a, 2017b; Feld et al., 2015; Kwo et al., 2017). DAA-based regimens are also well-tolerated and have limited contraindications. Consequently, the previous medical barriers to HCV treatment are diminishing (Grebely et al., 2017b). At the population level, mathematical models suggest scale-up of HCV treatment is cost-effective and can substantially reduce HCV morbidity and transmission, if coupled with direct prevention (Gountas et al., 2017; Martin et al., 2016; Stone et al., 2017).

Accordingly, in 2016, the World Health Organization (WHO) set a global target to eliminate viral hepatitis as a major public health threat by 2030 (WHO, 2016a). While direct prevention and increased screening initiatives will be key components of public health campaigns, the feasibility of HCV elimination is ultimately contingent upon massively expanding treatment coverage (WHO, 2016a, 2016b). The high cost of DAAs is undeniably a key barrier to this endeavor (WHO, 2016c). However, preferential pharmaceutical pricing contracts and generic production of relatively low-cost DAAs have permitted some countries to roll-out HCV elimination programs (e.g., Egypt and Georgia) (El-Akel et al., 2017; Gvinjilia, 2016). With increased and sustained political will and support, therapy costs for HCV infection are projected to continually decline-similar to what was previously seen with generic antiretroviral therapy (ART) for human immunodeficiency virus (HIV) infection (Hill, Simmons, Gotham, & Fortunak, 2016). Even so, challenges in achieving HCV elimination via 'treatment as prevention' will extend far beyond cost in marginalized populations such as PWID.

Globally, PWID have had poor uptake of HCV treatment (Alavi et al., 2015; Grebely et al., 2007; Iversen et al., 2017; Mehta et al., 2008), even in the DAA era (Spradling et al., 2017; Tsui et al., 2016; van Santen, van der Helm, Lindenburg, Schim van der Loeff, & Prins, 2017). In high-income countries, the high attrition from HCV diagnosis to initiation of HCV treatment among PWID can be explained by a multifactorial network of individual-, provider-, and system- and structurallevel barriers (Alavi et al., 2015; Doab, Treloar, & Dore, 2005; Fischer, Vasdev, Haydon, Baliunas, & Rehm, 2005; Grebely et al., 2011, 2008; Heimer et al., 2002; Kwiatkowski, Fortuin Corsi, & Booth, 2002; Mehta et al., 2008, 2005; Scheft & Fontenette, 2005; Sulkowski & Thomas, 2005; Treloar et al., 2011; Treloar, Hull, Dore, & Grebely, 2012; Wansom et al., 2017), some of which have not changed despite the availability of DAAs (Asher et al., 2016; Cope, Glowa, Faulds, McMahon, & Prasad, 2016; Falade-Nwulia, McAdams-Mahmoud, Irvin, Niculescu, & Page, 2016; Mah et al., 2017; Socias et al., 2017; Valerio, et al., 2018). There is a paucity of data on HCV treatment uptake and associated barriers among PWID in low-and-middle income countries (LMIC) (Alam-Mehrjerdi et al., 2016; Chu et al., 2016; Loewinger et al., 2016; Mukherjee et al., 2017; Souliotis, Agapidaki, Papageorgiou, Voudouri, & Contiades, 2017), particularly from Southern and Southeastern Asia (Wait et al., 2016). Preliminary evidence from this region suggests there is poor knowledge of HCV disease and treatment among PWID attending methadone clinics, needle-exchange programs, and rehabilitation centers (Chu et al., 2016; Loewinger et al., 2016; Mukherjee et al., 2017), which may be indicative of structural barriers related to treatment availability and cost, as well as of low patient readiness for HCV treatment (e.g., low awareness and perceived need for treatment). Individual-level indicators of HCV treatment readiness, such as treatment willingness and intentions, have not been fully examined among PWID in LMIC. Given that readiness at the individual level is a key factor in successful engagement in care and treatment for HCV (Alavi et al., 2015; Grebely et al., 2011), a lack of HCV treatment readiness among PWID in LMIC could undermine efforts to expand coverage of HCV treatment.

India is home to an estimated 164,820 to 1.1 million (predominantly male) PWID (Aceijas & Rhodes, 2007; Mathers et al., 2008),

with recent estimates of HCV mono-infection and HIV/HCV co-infection among PWID of 25.6% and 14.4%, respectively (Solomon et al., 2015). Although India has provided free government-sponsored ART programs for HIV infection since 2004, recent data suggest PWID in India lag behind other populations in linkage to HIV care and ART uptake, which is related to logistical barriers, stigma, and a lack of interest/readiness to initiate ART (McFall et al., 2016; Mehta et al., 2015). Comparable data on the HCV care continuum and associated barriers among PWID in India are limited. India has made strides to remove structural barriers to HCV treatment including the availability of low cost generic DAA medications. Specifically, in March 2015, sofosbuvir, a pan-genotypic DAA, was introduced into the Indian market (Puri et al., 2016). India subsequently leveraged a license from Gilead to produce 11 generic versions of sofosbuvir (Hill et al., 2016), and currently, four generic DAAs are available in India, including the pangenotypic fixed dose combination of sofosbuvir/velpatasvir and sofosbuvir combined with daclatasvir as individual tablets-all for approximately \$150 US dollars per course. However, additional structural barriers to HCV treatment access remain. Outside of Punjab, where the state government has launched a free treatment program (Dhiman, Satsangi, Grover, & Puri, 2016), most patients in India must pay for HCV treatment out-of-pocket (Puri et al., 2016), which includes not only the drug but the monitoring costs (e.g., HCV RNA testing). Additionally, to receive HCV treatment, patients must visit a medical gastroenterologist in settings that may not be favorable to PWID (Puri et al., 2016). Data on residual individual-level barriers to HCV treatment among PWID in India are needed.

In this study, we aimed to characterize the HCV care continuum, examine perceived barriers to HCV care, and identify factors associated with HCV knowledge, treatment willingness, and intent for specialist assessment among community-based PWID in Chennai, India. Of note, when data were collected, sofosbuvir was the only DAA available in India and the only available pan-genotypic regimens included 12 weeks of pegylated interferon, sofosbuvir and ribavirin, or 24 weeks of sofosbuvir and ribavirin. Given the ongoing challenges HIV-infected PWID face related to HIV care in this setting, we hypothesized that there may be HIV-related differences in barriers to HCV care and treatment.

Methods

Study population

Participants were recruited from an ongoing community-based cohort of current and former PWID in Chennai, India (The Chennai HIV, HCV and Eeral study [CHHEERS]), which has been previously described (Solomon et al., 2016). In brief, between February 2012 and July 2015, the study enrolled 1042 individuals through community outreach (355 [35.6%] were HCV-infected and 148 [14.8%] were HIVinfected). All participants provided informed consent, were ≥ 18 years of age, and self-reported injection drug use in the five years prior to enrollment. A convenience sample of 860 (83%) individuals were enrolled in longitudinal follow-up. At enrollment and at semi-annual visits, participants completed a structured electronic interviewer-administered questionnaire that collected information on sociodemographics, past and current substance use, and past medical care. Alcohol use was assessed using the Alcohol Use Disorders Identification Test (AUDIT) questionnaire (Babor, Higgins-Biddle, Saunders, Monteiro, & W.H. Organization, 2001; Saunders, Aasland, Babor, De la Fuente, & Grant, 1993). A measurement of liver stiffness was ascertained by transient elastography using a FibroScan machine at each visit (EchoSens, Paris, France) (Sandrin et al., 2003). Participants also underwent a blood draw at each visit. The study was approved by the Institutional Review Boards of the Johns Hopkins Bloomberg School of Public Health and YR Gaitonde Centre for AIDS Research and Education.

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