Poster # 641

Rapid Progression to Cirrhosis and Death Among HCV-Infected Persons Who Inject Drugs in India

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ABSTRACT (revised)

Background. The recent introduction of direct-acting antivirals for HCV have sparked hope for HCV treatment in resource-limited settings (RLS). Despite WHO recommending HCV therapy for all chronically infected persons, it is likely that initially, similar to the early years of ART, access to these therapies will be limited in RLS. Therefore, it is critical to identify HCV-infected persons most in need of therapy.

Methods. A cohort of 954 persons who inject drugs (PWID) was recruited from 2/2012 – 1/2015 in Chennai, India, of whom 366 were HCV antibody positive and 276 were chronically HCV-infected (HCV RNA positive). We characterized incidence of clinical outcomes (all cause-mortality and cirrhosis) among HCV-infected individuals with at least 1 follow-up visit or confirmed death (n=226). Cirrhosis was ascertained by elastography (Fibroscan) and all-cause mortality by verbal autopsy. Kaplan-Meier survival curves and Poisson regression were used to identify predictors. A subset was asked about barriers to accessing HCV treatment (n=62).

Results. Median age of HCV-infected persons was 42; all were male, 53% had primary school education or less and median monthly income was ~$97 USD. 84 (30%) were HIV/HCV co-infected. 49% had no fibrosis, 23% moderate fibrosis and 26% had severe fibrosis/cirrhosis at baseline. 55% had evidence of alcohol dependence by AUDIT. 32 died over a median 2 years – mortality rate [MR]: 7.8 per 100 person-years (PY). Mortality per 100 PY was 4.4 among HCV mono-infected and 14.4 among HIV/HCV co-infected persons (adjusted incidence rate ratio [aIRR]: 4.5; 95% confidence interval [CI]: 2.0, 10.1). Mortality was also higher in those with cirrhosis (aIRR: 2.0; 95% CI: 0.9, 4.4;) and those with alcohol dependence (aIRR: 2.7; 95% CI: 0.9, 7.8) though this did not achieve statistical significance. Among 152 without significant fibrosis/cirrhosis at baseline, 40 (26%) progressed to significant fibrosis/cirrhosis over a median of 2 years (IRR: 15.0 per 100 person-years). Overall, 21% reported being linked to care for hepatitis C, and 7% reported receiving treatment for hepatitis C with none achieving sustained virologic response. The primary reasons for not taking treatment were negative perceptions about treatment (e.g., side effects and low perceived efficacy; 50%) followed by cost (31%) and competing priorities (8%).

Conclusions. High mortality among HCV- and especially HIV/HCV-coinfected persons, low treatment uptake, and negative perceptions regarding interferon- based regimens underscore the importance of efforts to deliver all-oral HCV treatment in RLS.

BACKGROUND

- Globally, ~170 million persons are infected with hepatitis C virus (HCV)
- Little information is available from low-and-middle income countries, where >75% of HCV-infected individuals live and genotype 3 infection predominates
- In India, an estimated 15 million persons are infected with HCV
- Recent introduction of direct-acting antivirals for HCV has sparked hope for HCV treatment in resource-limited settings (RLS)
- Access to these therapies are limited in RLS
- There is a critical need to identify HCV-infected persons most in need of therapy

METHODS

STUDY POPULATION

- A convenience sample of 954 persons was recruited from February 2012 – September 2014 in Chennai, India
- All persons had to be ≥ 18 years of age, report a history of drug injection in the prior 5 years, and provide informed consent
- 366 (38%) were HCV antibody positive of whom 276 (29%) were chronically HCV-infected (HCV RNA positive)
- A subset answered a survey about barriers to HCV care (n=62)

STATISTICAL METHODS

- Liver stiffness cutoffs were based on US cohorts: <8 – no/mild fibrosis; 8-12.3 –moderate fibrosis; ≥12.3 – severe fibrosis/cirrhosis
- Kaplan-Meier survival curves and Poisson regression were used to identify independent predictors of mortality

ETHICAL CLEARANCES

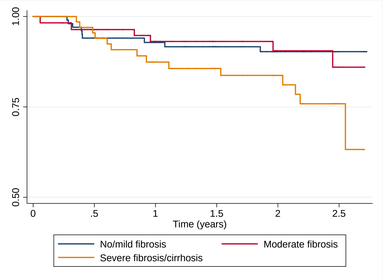
- This study was approved by the JHSPH, and the Y.R.G.CARE Institutional Review Boards

RESULTS

	HCV mono-infected (n= 192)*	HIV/HCV co-infected (n=84)*
Median age, (IQR)	43 (39-46)	40 (36-43)
Proportion male	192 (100)	84 (100)
Education		
None	29 (15)	22 (26)
Primary	61 (32)	33 (39)
Secondary	23 (12)	8 (10)
High school	44 (23)	19 (23)
Vocational/ college	35 (18)	2 (2)
Marital status		
Never married	38 (20)	27 (33)
Currently married	132 (69)	41 (49)
Widowed/Divorced/Separated	22 (11)	15 (18)
Median income in Indian rupees, (IQR)	6000 (4500-10000)	5000 (3750-6000)
Injected drugs in past 6 months	35 (18)	12 (14)
Alcohol use		
None/Limited use	58 (30)	24 (29)
Harmful/Hazardous use	24 (13)	14 (17)
Alcohol dependence	110 (57)	46 (55)
Median body mass index (kg/m^2)	21 (18-24)	19 (17-20)
Current antiretroviral therapy	N/A	29 (35)
Median CD4 cell count, (IQR)	N/A	351 (230-475)
Median Log$_{10}$ HCV RNA, (IQR)	6.3 (5.6-6.7)	6.5 (6.2-6.8)
HBsAg positive	12 (6)	2 (2)
Ever therapy for HCV	5 (3)	0 (0)
Fibrosis		
No/ mild fibrosis	88 (47)	47 (57)
Moderate	45 (24)	18 (22)
Severe fibrosis/ cirrhosis	54 (29)	18 (22)

Table I. Characteristics of persons by HIV status

*n (%) unless otherwise specified



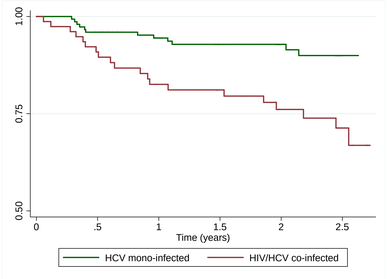


Figure I. Kaplan-Meier curves for all-cause mortality by HIV status and fibrosis

	Unadjusted		Adjusted	
	IRR	95% CI	IRR	95% CI
Age	1.38	0.80 - 2.38	1.43	0.77 – 2.64
Education level				
None	REF			
Primary	0.66	0.27 – 1.63		
Secondary	1.33	0.47 – 3.75		
High School	0.37	0.12 – 1.09		
Vocational/ college	0.33	0.07 – 1.54		
Alcohol use (AUDIT)				
Low	REF		REF	
Harmful or hazardous	1.51	0.36 – 6.33	1.19	0.26 – 5.53
Alcohol dependence	2.79	1.06 – 7.31	2.67	0.91 – 7.83
Injection drug use in prior 6 months	2.06	0.63 – 6.78		
HIV positive	3.24	1.57 – 6.68	4.49	2.0 – 10.1
CD4 cell count <200 (vs. ≥ *200)*	5.71	2.37 – 13.78		
log$_{10}$HIV RNA	1.58	1.13 – 2.22		
Ever HAART use	0.54	0.22 – 1.33		
Fibrosis				
No/ mild fibrosis	REF			
Moderate fibrosis	1.12	0.40 – 3.14		
Severe fibrosis/ Cirrhosis	2.34	1.01 – 5.40		
Severe fibrosis/ Cirrhosis (vs. no/mild/moderate)	2.24	1.08 – 4.64	2.05	0.94 – 4.44

Table 2. Unadjusted and adjusted predictors of mortality

IRR = Inter-rater reliability; CI = Confidence Interval; Highlighted variables are statistically significant

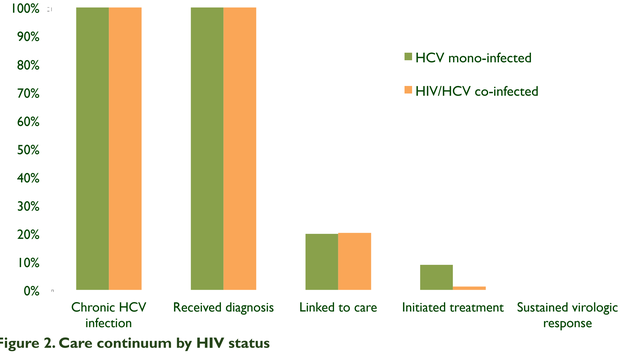


Figure 2. Care continuum by HIV status

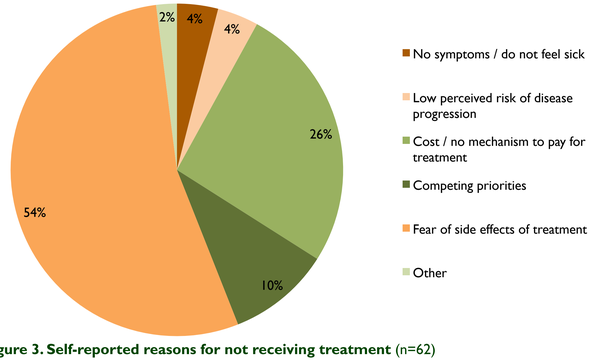


Figure 3. Self-reported reasons for not receiving treatment (n=62)

CONCLUSIONS

- In this Indian cohort of PWID, we observed an extremely high mortality rate particularly among those who were HIV/HCV co-infected.
- Mortality was also associated with cirrhosis and alcohol dependence.
- We observed limited access to HIV and HCV therapy in this population.
- Low HCV treatment uptake in this population may be driven by a combination of negative perceptions regarding interferon- based regimens and cost/unaffordability of regimens.
- Efforts need to be made to improve access all-oral therapies for HCV in resource-limited settings.

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