The Effects of Alcohol on Spontaneous Clearance of Acute Hepatitis C Virus Infection in Females versus Males

Judith I. Tsui[1], Ali Mirzazadeh[2], Judith A. Hahn[2], Lisa Maher[3], Julie Bruneau[4], Jason Grebely[3], Margaret Hellard[5], Arthur Y. Kim[6], Naglaa H. Shoukry[4], Andrea L. Cox[7], Maria Prins[8], Gregory Dore[3], Georg Lauer[6], Andrew Lloyd[3], Kimberly Page[9] on behalf of the InC3 Collaborative

[1]University of Washington, Seattle, WA, USA; [2]University of California, San Francisco, CA, USA; [3]University of New South Wales, Sydney, Australia; [4]Université de Montréal, Montréal, QC, Canada; [5]Burnet Institute, Melbourne VIC, Australia; [6]Harvard Medical School, Boston, MA, USA; [7]Johns Hopkins Medical Institutions, Baltimore, MD, USA; [8]GGD Public Health Service of Amsterdam, Amsterdam, The Netherlands; [9]University of New Mexico Health Sciences Center, Albuquerque, New Mexico, USA

Introduction

- Approximately one quarter of persons exposed to hepatitis C virus (HCV) will spontaneously clear infection.
- Female sex and IFNL4 genotype has been shown to predict clearance.
- The impact of alcohol on HCV clearance is less well understood, and sex-specific effects are unknown.

Specific Aims

1) To evaluate the impact of drinking alcohol on likelihood of HCV spontaneous clearance among persons with documented acute HCV who were prospectively followed over time with repeated measures of HCV viral load and drinking self-report.

2) To explore whether associations between alcohol and spontaneous clearance differed among women compared to men.

Methods

- Prospective observational study using data from The InC3 study, a collaboration of nine cohorts in the United States, Australia, Canada, and The Netherlands.
- Persons who injected drugs were prospectively followed between 1979-2012.
- Study visits occurred every 1-6 months and included HCV testing (anti-HCV and HCV RNA testing).
- Predictor: alcohol use (yes/no) at the time of infection .
- Outcome: spontaneous clearance (i.e. two consecutive undetectable HCV RNA test results greater than or equal to four weeks apart after date of acute infection).
- The effects of alcohol use on time to HCV clearance were assessed by Kaplan-Meier curves. Patients who died or were lost to follow-up were censored at their last visit.
- Cox proportional hazards analysis were used to assess the independent effects of alcohol, adjusting for age, race/ethnicity, site, and IFNL4 status on HCV spontaneous clearance.
- To assess the effects of sex, we included an interaction term between sex and alcohol use and estimated both male- and female-specific adjusted hazard ratios using the post

Results

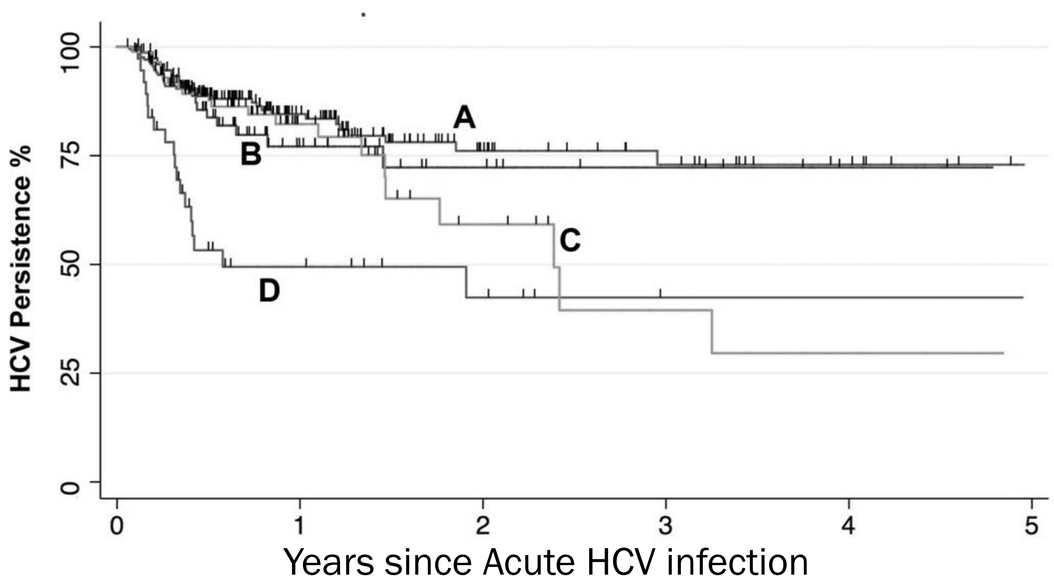
- There were 411 participants with acute HCV and data on concomitant alcohol use.
- Alcohol use did not differ by age, sex, race/ethnicity, HCV genotype, or IFNL4 genotype.

Table 1 Rates of spontaneous clearance of HCV infection (per 100 person-years observation) among drinkers and non-drinkers of alcohol, stratified by sex.

Sub-group	Drinking status	SC cases	pyo	Incidence/100 pyo (95% CI)	RR (95% CI)	P-value
Overall						
	Non-drinkers	33	153.5	21.5 (15.3, 30.2)	1.0	0.04
	Drinkers*	56	407.2	13.8 (10.6, 17.9)	0.6 (0.4, 0.9)	
Males						
	Non-drinkers	15	108.1	13.9 (8.4, 23.0)	1.0	0.69
	Drinkers	35	284.3	12.3 (8.8, 17.1)	0.9 (0.5, 1.6)	
Females						
	Non-drinkers	18	44.8	40.1 (25.3, 63.7)	1.0	0.007
	Drinkers	21	123.0	17.1 (11.1, 26.2)	0.4 (0.2, 0.8)	

SC: Spontaneous Clearance; RR: Rate Ratios calculated with the Mantel-Haenszel method; PYO: Person-years of observations; CI: Confidence Interval.
*Alcohol drinking status at or after acute HCV infection.

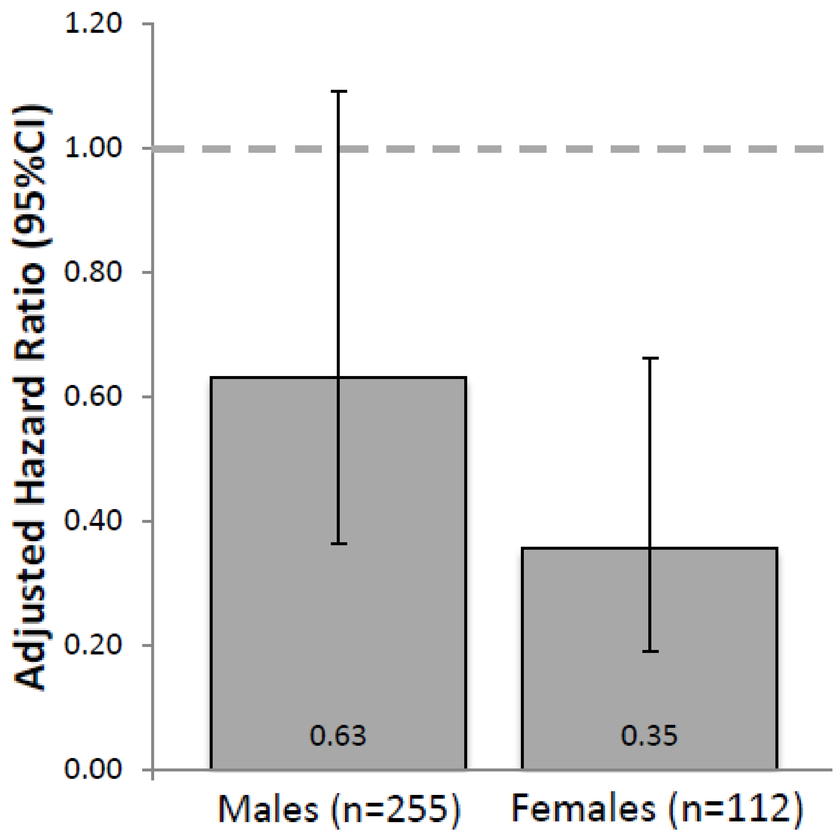
Figure 1 Kaplan Meier curves of HCV persistence by sex and alcohol-drinking status at or after HCV acute infection.



Number at risk						
A. Drinker, Males	207	80	34	23	15	9
B. Non-drinker, Males	78	25	12	8	4	3
C. Drinker, Females	88	29	9	4	3	3
D. Non-drinker, Females	37	11	6	2	2	2

0 1 2 3 4 5
Years since Acute HCV infection

Figure 2 Adjusted* relative hazards for spontaneous clearance associated with drinking alcohol in females versus males.



*Models adjusted for age, race/ethnicity, IFNL4, and study site.

Results

- The test of homogeneity for gender for the effect of alcohol on HCV clearance (i.e., test for interaction) was statistically significant ($\chi 2 = 27.3$, $p<0.001$).

Limitations

- Data on frequency/ amounts of alcohol used by participants was asked in different formats and not available for the full sample; analyses of dose response not possible.
- Alcohol use was based on self-report and, thus, could be subject to social desirability bias.
- The absolute number of outcomes of spontaneous clearance is modest. As such, sex-specific results should be interpreted cautiously and confirmed in other samples.

Conclusions

- This prospective study of HCV clearance among people with acute infection found that self-reported alcohol use was associated with a lower relative hazard of spontaneous clearance, and sex-stratified analyses suggested strong and significant associations among women only.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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