Semen HCV RNA level may mirror dynamics of blood HCV RNA in HIV-positive men with acute HCV infection

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Aim

We hypothesise that raised semen HCV RNA levels in acute HCV infection may contribute to sexual transmission of HCV in HIV-positive men.

Methods

Men with recent and acute (AHCV, ≤ 12 months' duration) and chronic (CHCV, >12 months) HCV infection were prospectively recruited. Participants completed a questionnaire providing clinical and demographic information. Paired EDTA plasma and semen samples were collected at two time points. STI screens were performed Semen was separated into plasma and cellular fractions through centrifugation. The Abbott M2000 RT-PCR was optimised for quantification of HCV RNA in seminal plasma and cell pellet. Lower limit of detection was 60 IU/mL. Statistical significance was assessed using Chi-squared, Fishers Exact, Mann-Whitney U and Kruskal-Wallis tests with $p < 0.05$ considered significant.

Results

Baseline cohort characteristics are described in Table 1. Overall 29/66 (43.9%) of men had detectable HCV RNA in semen at baseline. Fifty-six men underwent an STI screen at baseline and 11 (19.6%) had an STI diagnosed. When detected, median semen HCV RNA was 2.1 (IQR 1.8-2.6) log IU/mL. HCV RNA levels in blood and seminal plasma were correlated (r^2=0.142) (Fig. 1). There was a similar proportion of men with detectable semen HCV comparing AHCV versus CHCV (p=0.613) or HIV-positive versus HIV-negative (p=0.191). There was no significant difference in median blood HCV RNA comparing AHCV/HIV+, CHCV/HIV+ and CHCV/HIV- (p=0.055). Factors associated with presence of HCV RNA in seminal plasma are shown in Table 2. Blood HCV RNA was the only factor predictive of seminal RNA shedding.

	AHCV/HIV+	CHCV/HIV+	CHCV/HIV-	All
Number of men	18 (30.0)	22 (36.7)	26 (43.3)	66 (100)
Median age, years	45.3 (36.5-49.0)	49.7 (43.9-54.3)	52.1 (46.8-56.0)	49.0 (43.8-53.3)
Australian born	13 (72.2)	18 (81.8)	19 (73.1)	50 (75.8)
MSM	18 (100)	21 (95.5)	7 (26.9)	46 (69.7)
Route of HCV acquisition				
Injection drug use	8 (44.4)	19 (86.4)	15 (57.7)	42 (63.6)
Sexual	10 (55.6)	3 (13.6)	3 (11.5)	16 (24.2)
Median blood HCV RNA, log IU/mL	5.8 (4.4-6.2)	6.4 (5.5-6.7)	6.1 (5.6-6.4)	6.1 (5.5-6.5)
HCV genotype				
1a	10 (55.6)	16 (72.7)	13 (50.0)	39 (59.1)
3a	5 (27.8)	3 (13.6)	9 (34.6)	17 (25.8)
Median Fibroscan score, kPa	6.6 (6.1-8.6)	7.0 (5.7-12.2)	9.7 (6.9-14.3)	7.6 (6.1-11.8)
Median volume of seminal plasma, mL	1.0 (0.5-1.3)	1.0 (0.5-1.5)	1.0 (0.4-1.5)	1.0 (0.5-1.5)
Median CD4 cell count, cells/mm^3	576.0 (337.0-715.8)	643.5 (455.5-1105.0)	NA	598.0 (409.5-787.5)
Number receiving cART	15 (83.3)	20 (90.9)	NA	35 (87.5)
No. on cART with HIV-1 RNA <50 IU/mL	12 (80.0)	20 (100)	NA	32 (80.0)
Median ALT, U/L	121.5 (60.0-374.3)	75.5 (42.5-139.8)	86.5 (47.8-171.0)	91.0 (47.8-174.0)
Infectious syphilis	3 (16.7)	2* (9.1)	0	5 (7.6)
Full STI screen performed	16 (88.9)	20 (90.9)	20 (76.9)	56 (84.8)
Non-LGV chlamydia	3 (18.8)	0	0	3 (5.4)
LGV	0	1* (5.0)	1 (5.0)	2 (3.6)
HSV	2 (12.5)	0	0	2 (3.6)
Any STI	8 (50.0)	2 (10.0)	1 (5.0)	11 (19.6)

Table 1. Baseline cohort characteristics. Brackets denote IQR or %. *one man had LGV and syphilis

Results

Figure 1. Seminal plasma HCV RNA level according to blood HCV RNA level

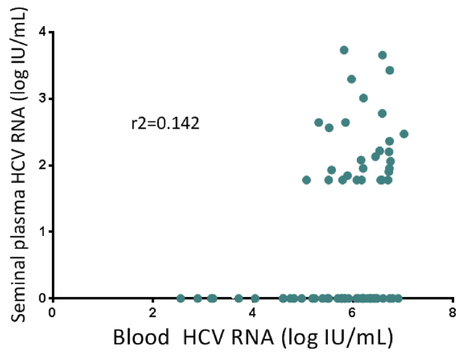


Figure 2. Detection of HCV RNA in seminal plasma according to blood HCV RNA. Error bars indicate median and IQR.

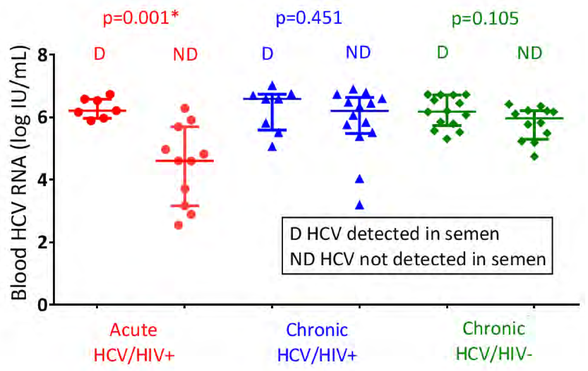
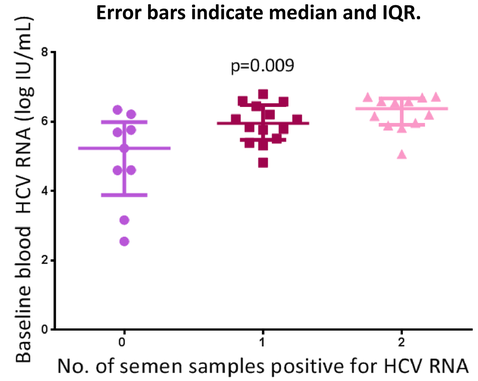


Figure 3. Longitudinal shedding of HCV RNA in semen. Error bars indicate median and IQR.



Results

	HCV RNA in Seminal Plasma		
	Present	Absent	p value
Number of individuals	29 (43.9)	37 (56.1)	
Age, years	49.8 (44.8-53.0)	48.2 (43.7-55.0)	0.736
HIV-infected	15 (51.7)	25 (67.6)	0.191
Acute HCV	7 (24.1)	11 (29.7)	0.613
Median duration of AHCV, weeks	13.7 (7.7-22.4)	9.1 (5.4-29.5)	0.783
Median blood HCV RNA, log IU/mL	6.2 (5.8-6.7)	5.8 (4.8-6.3)	0.002*
HIV parameters			
CD4 cell count, cells/mm^3	580.0 (324.0-754.0)	663.0 (451.0-1017.0)	0.170
HIV RNA < 50 IU/mL	11 (73.3)	21 (84.0)	0.444
HCV genotype			
1a	15 (51.7)	24 (64.9)	0.281
3a	8 (27.6)	9 (24.3)	0.764
Median volume of seminal plasma, mL	1.1 (0.5-2.3)	0.90 (0.5-1.4)	0.143
Median Fibroscan score, kPa	7.6 (6.2-13.6)	7.8 (6.1-11.8)	0.705
Infectious syphilis	1 (4.0)	4 (12.9)	0.367
Any STI	3 (12.0)	8 (25.8)	0.319
Sexual mode of HCV acquisition	6 (20.7)	10 (27.0)	0.551

Table 2. Factors associated with detection of HCV RNA in seminal plasma. Brackets denote IQR or %. * p<0.05

Median blood HCV RNA was higher in men with detected versus undetected seminal plasma RNA for AHCV/HIV+ (6.2, IQR 6.0-6.7 versus 4.6, IQR 3.2-5.7 log IU/mL p=0.001) but not for CHCV/HIV+ or CHCV/HIV- (Fig. 2). Of 11 men for whom both seminal plasma and pellet were assayed, four (36.4%) had detectable RNA in pellet and six (54.5%) in seminal plasma. In all cases, reduced detection of HCV RNA in seminal pellet versus seminal plasma was observed. Thirty-five men (53.0%) attended a follow up visit at a median 18.0 (IQR 14.6-25.6) weeks post enrolment. Nine men undetectable for seminal plasma HCV RNA at baseline became detectable at follow up. Prolonged shedding of HCV RNA in seminal plasma was more likely for men with a higher baseline blood RNA (see Fig. 3). A relationship was also observed for longitudinal shedding in men with AHCV: blood RNA for men with 2, 1 and 0 specimens positive was 6.0, IQR 5.9-6.2, 6.2, IQR 4.8-6.6 and 4.6, IQR 2.9-5.2 log IU/mL respectively (p=0.019). However, there was no significant difference in blood RNA levels in men with CHCV according to number of semen specimens detectable for HCV RNA (p=0.177).

Conclusion

A minority of men had detectable HCV RNA in semen at baseline but a majority of those attending follow up had RNA detectable in semen for at least one visit. Semen HCV RNA levels were generally low. However, the relationship between plasma and semen HCV RNA in HIV-positive men with acute HCV indicates a potential for heightened infectiousness in the setting of high early infection HCV RNA levels.

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