

Use of Serum Markers to Assess Progression of Liver Disease in HIV HCV Co-infected Women

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Background

- Co-infection with Hepatitis C (HCV) is increasingly recognized as a cause of morbidity and mortality in HIV infected individuals
- Women with HCV have been shown to have milder and less progressive liver disease than men
- Most studies of HIV and HCV have predominantly studied co-infection in males

Aims

- To assess liver disease in a cohort of women with HIV and HCV
- To assess the relationship between serum markers and all-cause mortality among women with HIV who were co-infected with HCV

Methods

- Women's Interagency HIV Study (WIHS)
 - NIH funded prospective, multicenter, cohort study of women with, or at risk for, HIV infection
- Subjects seen every 6 months
- Serum markers of fibrosis were evaluated by APRI and FIB-4
- HCV antibody status was assessed at enrollment
- Laboratory and clinical data measured q 6 months
- Associations with clinical outcome of all-cause mortality

Calculating APRI & FIB-4

$$APRI = \frac{AST}{AST_{ULN}} * \frac{100}{platelet}$$

$$FIB - 4 = \frac{AST}{\sqrt{ALT}} * \frac{age}{platelet}$$

where , *AST = Aspartate aminotransferase*

ULN = Upper limit of Normal

ALT = alanine aminotransferase

Exclude : 1) AST and ALT > 10xULN (Acute Hepatitis)

2) Platelet counts < 25k/ μ L (Thrombocytopenia)

Study Population

- Women's Interagency HIV Study (WIHS)
 - N=3168 women with at least 2 valid APRI/FIB-4 scores
 - 760 HIV Mono-Infected women
 - 516 HIV/HCV Co-Infected women
- Time Points Studied
 - enrollment
 - yearly over 5 and 10 years
 - last available serum sample

Baseline Characteristics N=3168

Age, years	35 [29-40]
Race, % (n)	
Caucasian	14% (448)
African-American	56% (1770)
Hispanic	26% (833)
Other	3% (106)
Years of Follow-up	5.7 [3.9-11.0]
Observations per ID	9 [5-14]
HCV Ab positive, % (n)	31% (991)
HIV positive, % (n)	74% (2354)
HBsAg Status, % (n)	
Negative	81% (2547)
Negative, latent infection	17% (548)
Active/ Chronic Infection	2% (64)

* Median [IQR], unless otherwise noted

FIB-4

<i>Baseline</i>	n	<1.5	>1.5 to <3.25	>3.25
HIV +	760	678 (88.2%)	71 (10.4%)	11 (1.4%)
HIV + / HCV+	516	327 (63.4%)	160 (31%)	29 (5.6%)
<i>5 years</i>				
HIV +	731	619 (82.5%)	96 (15.5%)	16 (2%)
HIV + / HCV+	506	245 (48.6%)	193 (38%)	68 (13.4%)
<i>10 years</i>				
HIV +	566	478 (84.5%)	72 (12.7)	16 (2.8%)
HIV + / HCV+	345	142 (41%)	152 (44%)	51 (14.8%)

Baseline vs. Last APRI

HCV Positive at Baseline=991

		n	Last APRI		
			Low	Medium	High
Baseline APRI	Low, <0.5	529	67%	25%	7%
	Medium, 0.5-1.5	373	31%	46%	23%
	High, >1.5	89	11%	37%	52%

HCV Negative at Baseline, n=2177

		n	Last APRI		
			Low	Medium	High
Baseline APRI	Low, <0.5	1963	93%	6%	1%
	Medium, 0.5-1.5	188	68%	27%	5%
	High, >1.5	26	58%	31%	12%

Baseline vs. Last FIB4

HCV Positive at Baseline=991

		n	Last APRI		
			Low	Medium	High
Baseline APRI	Low, <1.5	620	60%	28%	12%
	Medium, 1.5-3.25	290	18%	52%	30%
	High, >3.25	81	11%	22%	67%

HCV Negative at Baseline, n=2177

		n	Last APRI		
			Low	Medium	High
Baseline APRI	Low, <1.5	2028	91%	8%	2%
	Medium, 1.5-3.25	128	52%	36%	12%
	High, >3.25	21	43%	33%	24%

APRI in those who died

	HIV+ HCV-	HIV+HCV+
Baseline	218	321
Minimal, <0.5	154 (71%)	140 (44%)
Moderate, 0.5-1.5	52 (24%)	132 (41%)
Severe, >1.5	12 (6%)	49 (15%)
Last available		
Minimal, <0.5	135 (62%)	120 (37%)
Moderate, 0.5-1.5	63 (29%)	100 (31%)
Severe, >1.5	20 (9%)	101 (31%)

Predictors of all-cause mortality in all WIHS- multivariate analysis

Predictor	HR	[95%CI]
• HIV	4.0	[2.7-5.7]
• Baseline APRI (severe)	2.7	[2.0-3.7]
• Baseline APRI (moderate)	1.5	[1.2-1.8]
• HCV	1.8	[1.4-2.1]
• HBV	1.7	[1.1,2.7]
• age per 10 year increase	1.4	[1.3-1.6]
• heavy alcohol	1.0	[0.8,1.4]
• HAART	0.8	[0.7-1.0]
• Obesity	0.8	[0.6-0.9]

Conclusions

- Women co-infected with HCV had more progressive liver disease than those with HIV alone
- By these indirect methods, nearly half of the coinfecting women had not progressed over 5 years and 41% had not progressed over 10 years
- Among the HIV HCV infected women who died, 38% had severe fibrosis/cirrhosis as estimated by FIB-4 or APRI
- This suggests that while the majority of women have mild disease, liver disease progression is important in morbidity and mortality in HIV+ HCV+ women
- Further research on factors associated with liver disease progression is warranted