

The Natural History of Hepatic Steatosis among HIV/HCV Co-infected Patients with Paired Liver Biopsy

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ABSTRACT

Background: The natural history of hepatic steatosis among HIV/HCV coinfected patients (pts) in the era of potent antiretroviral therapy (ART) is unknown. We prospectively examined the change in steatosis grade between paired liver biopsies (bxs) among HIV/HCV coinfected pts attending an urban HIV clinic.

Methods: 57 coinfected individuals underwent two liver bxs. Paired bxs were simultaneously evaluated by a single pathologist who was blinded to bx sequence and scored: grade 0 none, 1 fat involving < 5% of hepatocytes, 2 5% to < 30%, 3, 30% to 60%, 4 > 60%. Clinical and laboratory data were collected from charts and the lab database. Alcohol assessment was computer-assisted. Logistic regression analysis was performed to determine correlates of steatosis change. Factors considered in analysis included demographics, alcohol, ART, liver enzymes over time, hepatic necroinflammatory activity and fibrosis.

Results: Characteristics at or prior to 1st bx: median age, 44 years (yrs); male, 70%; African-American, 69%; median weight, 139 pounds; CD4 < 200/mm³, 15%; HIV RNA < 400 c/mL, 60%; ART, 84%; alcohol abuse, 28%; persistently elevated ALT, 33%; hyperglycemia, 13%; hypertriglyceridemia, 26%; HCV genotype 1, 98%. Median time between bxs was 2.84 yrs (IQR, 2.04– 3.4 yrs). No steatosis change was observed in 33 pts (58%) whereas 1 grade increase occurred in 15 pts (26%) and 21 grade decrease occurred in 9 pts (16%).

Steatosis grade, 1st Bx (n, %)

Steatosis 2nd Bx	0	1	2	3
0	27 (67) (42)	1 (25)	0	3
1	13 (33) (42)	2 (50)	1 (100)	0
2	0	2 (16)	1 (25)	0

Compared to those with no change or decrease, pts with steatosis increase were more likely to have used dAT within 2 yrs of the 2nd bx (47% > 24%, P=09). No significant association was detected between progression of steatosis and time between bxs, age, gender, alcohol use, ALT or glucose level, other ART use, HIV suppression, or CD4 cell count. Fibrosis progression between bxs was not associated with steatosis at 1st bx or change between bxs.

Conclusions: Over a 3-yr interval, no patient experienced a > 1 grade increase in steatosis, and the majority (74%) had stable or decreased steatosis. Furthermore, steatosis was not prospectively associated with progression of hepatic fibrosis. Finally, while we observed a trend toward worsening steatosis with recent dAT use, further research is required to determine the relationship of steatosis, ART and metabolic disease.

BACKGROUND/OBJECTIVE

Hepatic steatosis has been associated with liver fibrosis and the use of specific antiretroviral drugs (e.g., stavudine) in HIV/hepatitis C virus (HCV) co-infected patients. However, the natural history of hepatic steatosis among HIV/HCV coinfected patients in the era of potent antiretroviral therapy (ART) is unknown

The objective of this investigation was to prospectively examine the change in steatosis grade between paired liver biopsies (bxs) among HIV/HCV coinfected adults attending an urban HIV clinic.

METHODS

Study subjects. Subjects for this investigation are 57 HIV/HCV coinfected members of the Johns Hopkins HIV clinic who had at least two liver biopsies.

Design. We conducted a prospective analysis of the histologic steatosis grade at biopsy 1 and 2.

Histology. Biopsies were evaluated by a single pathologist who was blinded to biopsy sequence and steatosis was characterized according to the percentage of hepatocytes affected: Grade 0, none with fat; 1, <5% fat; 2, 5-30% fat; 3, 30-60% fat; 4 > 60% fat

Demographic, clinical and laboratory data were collected from patient charts and the lab database. Alcohol assessment was computer-assisted at baseline and between biopsies. Antiretroviral drug exposure was prospectively captured from medical charts and pharmacy records.

Analysis. Prevalence of steatosis at biopsy 1 and 2 were compared using chi square tests. Univariate logistic regression was performed to determine correlates of steatosis change. Factors considered in analysis included demographics, alcohol, ART, liver enzymes over time, hepatic necroinflammatory activity and fibrosis.

RESULTS

Characteristics of the study population (n = 57 subjects) are shown in table 1. The prevalence of steatosis (any grade) on biopsy 1 was 30% and only 5 patients had steatosis affecting more than 5% of hepatocytes (Figure 1). The second liver biopsy was performed at a median interval of 2.84 years (IQR 2.04 – 3.41). At biopsy 2, the majority (74%) of patients had no change or a decrease in the amount of steatosis observed (Figure 2) and no patients had more than a 1 grade increase in steatosis. Among those with no fat on biopsy 1, 33% developed grade 1 steatosis (Figure 3) and among those with grade 1 steatosis, 42% had no fat on biopsy 2 (Figure 4). Characteristics of those with and without an increase in steatosis grade are shown in Table 2.

Table 1. Characteristics of study population at first biopsy

	N (%) N = 57
Median age, years (IQR)	44 (41-47)
Male gender	39 (70)
African-American Race	48 (85)
HCV genotype 1	56 (98)
Median body weight, pounds (IQR)	139 (113-185)
History of alcohol abuse	16 (28)
Hyperglycemia (random BG > 200)	(13)
Hypertriglyceridemia	(26)
History of injection drug use	38 (64)
CD4 cell count < 200 cells/uL	10 (18)
HIV RNA < 400 copies/ml	33 (60)
ART	48 (84)
Stavudine	12 (36%)

Figure 1. Prevalence of steatosis at biopsy 1

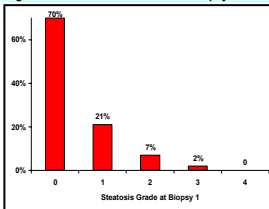


Figure 2. Change in steatosis grade between biopsy 1 + 2

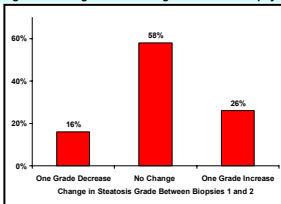


Figure 3. Steatosis grade at biopsy 2 among patients with no steatosis at biopsy 1

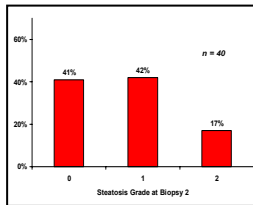


Figure 4. Steatosis grade at biopsy 2 among patients with grade 1 steatosis at biopsy 1

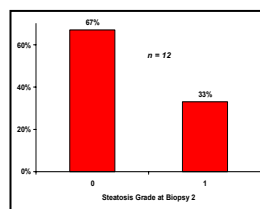


Table 2. Characteristics of persons with and without an increase in steatosis grade between biopsies 1 and 2

	No Change or Decrease 1 Grade N = 42	Increase 1 grade N = 15
At Biopsy 1		
Age, median years (IQR)	43 (40 – 47)	45 (42 – 48)
Female gender	22%	33%
African-American race	84%	93%
Weight>190 pounds	21%	7%
History of alcohol abuse	26%	33%
Glucose > 200 mg/dL	12%	29%
Cholesterol > 200 mg/dL	18%	31%
Diabetes (clinical diagnosis)	23%	38%
PI use	61%	40%
Stavudine within 2 years	24%	47%
Between Biopsies 1 and 2		
Fibrosis > 2 stage increase	28%	28%
Any PI use	71%	47%
Time on PI, years	1.86 (0 -1.83)	0 (0 – 2.48)
Stavudine use	38%	53%
Time on dAT, years	0 (0 – 0.45)	0.17 (0 – 1.4)
Weight > 190 pounds at bx 2	26%	20%
Cholesterol > 200 mg/dL	23%	20%
Triglyceride > 200 mg/dL	34%	50%
Glucose > 200 mg/dL	16%	33%
HCV therapy	33%	26%
> 75% HIV RNA improvement c/mL	60%	29%

CONCLUSIONS

Over a ~ 3-yr interval, no patient experienced a > 1 grade increase in steatosis, and the majority (74%) had stable or decreased steatosis. Furthermore, steatosis was not prospectively associated with progression of hepatic fibrosis. Finally, while we observed a trend toward worsening steatosis with recent dAT use, further research is required to determine the relationship of steatosis, ART and metabolic disease