Update on HIV-HCV Epidemiology and Natural History

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Learning Objectives

Upon completion of this presentation, learners should be better able to:

- Describe the burden of liver disease related to HCV among HIV-infected individuals
- Identify the factors influencing liver disease progression among HIV-HCV coinfected patients
Faculty and Planning Committee

Disclosures
Please consult your program book.

Off-Label Disclosure
There will be no off-label/investigational uses discussed in this presentation.

*Adapted from D:A:D Study Group. AIDS 2010, 24: 1537-1548*
Chronic HCV Epidemiology

• Worldwide: ~3% (170 million) chronically infected
  – Global prevalence varies depending on area
  – Up to 20% in highly endemic areas such as Nile Delta
  – 5 million are HIV-HCV coinfected

• United States: 1.3-1.9% (2.7-3.9 million) chronically infected with HCV
  – 8% are HIV-infected
  – 25-30% of HIV+ in US are also HCV+: prevalence varies by transmission risk factor

Global Prevalence of HCV

Which of the following is the most efficient mode of HCV transmission?

1. Heterosexual contact
2. Injection drug use
3. Maternal-child transmission
4. Male homosexual contact
Transmission of HCV

- Injection drug use 60%
- Sexual 15%
- Transfusion (before screening) 10%
- Other* 5%
- Unknown 10%
- Mother-child transmission 2-5% if mother is HCV-monoinfected and 5 x higher if mother is HIV-HCV-coinfected

* Iatrogenic; health-care work perinatal

Prevalence of HIV-HCV by HIV Risk Factor

Incidence of Acute HCV by Age Group- United States, 2000-2010

Reported cases/100,000 population

Source: National Notifiable Diseases Surveillance System (NNDSS)
Acute HCV Among HIV+ MSM

• 2004/2005: Clusters of acute HCV in HIV+ MSM reported in Northern Europe
  – Ulcerative STI’s more common in HCV incident cases
  – Molecular genetics more similar to each other than in IDU-associated HCV isolates

• Linkages made to high-risk sexual behavior (fisting, group sex, traumatic and receptive intercourse) and recreational (not-injected) drugs

Acute HCV Among HIV+ MSM

- Clusters of acute HCV among HIV+ MSM reported in both US and Australia

- Northern Europe cohort studies suggests increased HCV incidence since 2000
  - Short time frame (<2 years) between HIV diagnosis and HCV seroconversion

Hoofnagle, *Hepatology*. 1997;26:15S.


HIV impacts which of the following among HCV-infected individuals?

1. Clearance of acute HCV infection
2. Progression to cirrhosis
3. Survival after development of cirrhosis
4. Graft and patient survival after liver transplant
5. All of the above
Natural History of HCV

Acute HCV
- Resolved: 15-40%
- Stable: 85-90%

Chronic HCV
- 60-85%

Cirrhosis
- 10-15%

HCC
- Liver failure: 25% (2-4%)

Liver failure: 25%

Lower rates of spontaneous clearance

Influence of HIV on Spontaneous Clearance of HCV

Natural History of HCV

Acute HCV
- Resolved: 15-40%
- Stable: 85-90%

Chronic HCV: 60-85%
- Slowly progressive: 75%
- Cirrhosis: 10-15%

Increased risk of:
- Cirrhosis
- Liver decompensation
- Accelerated fibrosis progression
- HCC: Liver failure 25% (2-4%)

Increased Risk of Cirrhosis and ESLD Due to HIV-HCV Coinfection

**Histologic Cirrhosis**
- **Relative Risk**

- **Makris (UK)**: 0.76
- **Soto (Spain)**
- **Pol (France)**
- **Benhamou (France)**
- **Combined**: 10.83

**Decompensated Liver Disease**
- **Relative Risk**

- **Eyster (USA)**
- **Telfer (UK)**
- **Makris (UK)**
- **Lesens (Canada)**
- **Combined**: 10

Hepatocellular Carcinoma in HIV-HCV Coinfected Patients

Incidence density rate of HCC, cases per 1000 person years

Natural History of HCV

Acute HCV
- Resolved: 15-40%
- Stable: 85-90%

Chronic HCV: 60-85%
- Slowly progressive: 75%
- Cirrhosis: 10-15%
- HCC: Liver failure (25%, 2-4%)
  - Liver Transplant
  - Death: Shorter survival after decompensation
HIV-HCV Coinfected Patients with Decompensated Cirrhosis Shorter Survival

- Retrospective study of 1,037 HCV monoinfected and 180 HIV-HCV coinfected subjects with decompensated cirrhosis
- Median survival
  - HCV monoinfected: 48 months
  - HIV-HCV coinfected: 16 months
- Relative risk of death
  - HIV: 2.26 [1.51-3.38]

Natural History of HCV

Acute HCV
- Resolved: 15-40%

Chronic HCV
- Stable: 85-90%
- Cirrhosis: 10-15%
- Slowly progressive: 75%
- HCC Liver failure: 25% (2-4%)

Liver Transplant
- Poorer outcomes after liver transplant

Death
Liver Transplant and HIV-HCV

- Graft and patient survival is decreased among HCV+ transplant recipients.
  - Further reduced among HIV-HCV coinfected recipients.

![Graphs showing patient survival](image)

Spain Multi-site study
HIV-HCV: n=84

US Multi-site study
HIV-HCV: n=89

Which of the following factors has NOT been associated with higher risk of cirrhosis in HCV-infected individuals?

A. HCV Genotype
B. Alcohol use
C. Marijuana use
D. Post-menopausal status
E. Older age at time of HCV exposure
Risk Factors for Disease Progression in HCV-monoinfection

- Alcohol use
- Daily marijuana use
- Elevated BMI, obesity, insulin resistance
- Longer duration of infection
- Age >40 at time of infection
- Male gender, post-menopausal women
- Host genetic factors
- Organ transplantation
- Coinfections: HBV, HIV, Schistosomiasis
Predictors of Severe Liver Fibrosis in HIV-HCV Coinfected Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at biopsy &gt;35 years</td>
<td>2.95 (2.08-4.18)</td>
</tr>
<tr>
<td>Alcohol &gt;50 g/day</td>
<td>1.61 (1.1-2.35)</td>
</tr>
<tr>
<td>CD4 count &lt;500 cells/mm³</td>
<td>1.49 (1.06-2.08)</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.26 (0.94-2.06)</td>
</tr>
</tbody>
</table>

- 914 HIV-HCV coinfected patients with elevated ALT who underwent liver biopsy between 1992-2002
- Route of transmission, HCV genotype, HCV viral load, and ART were not associated with liver fibrosis severity

Alcohol and Liver Disease in HIV+ Patients

Percent of deaths due to ESLD

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-HCV-HBV</td>
<td>44%</td>
</tr>
<tr>
<td>HIV-HCV</td>
<td>31%</td>
</tr>
<tr>
<td>HIV-HBV</td>
<td>22%</td>
</tr>
<tr>
<td>HIV only</td>
<td>2%</td>
</tr>
</tbody>
</table>

Percent of ESLD deaths with history of excessive alcohol*

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-HCV-HBV</td>
<td>56%</td>
</tr>
<tr>
<td>HIV-HCV</td>
<td>62%</td>
</tr>
<tr>
<td>HIV-HBV</td>
<td>21%</td>
</tr>
<tr>
<td>HIV only</td>
<td>100%</td>
</tr>
</tbody>
</table>

*men >30 g/day, women >20 g/day

Hepatic Steatosis is Common in HIV-HCV Coinfected Patients

- Prevalence estimates range from 23-72%
- Factors associated with increased prevalence of hepatic steatosis in HIV-HCV coinfected patients:

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>1.13 (1.07, 1.19)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>2.32 (1.32, 4.07)</td>
</tr>
<tr>
<td>Elevated ALT</td>
<td>1.28 (1.02, 1.61)</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>1.67 (1.20, 2.34)</td>
</tr>
<tr>
<td>Necroinflammation</td>
<td>1.72 (1.11, 2.67)</td>
</tr>
</tbody>
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Impact of ART on Fibrosis Progression Rate (FPR) in HIV-HCV

- FPR similar among HIV-HCV coinfected patients with suppressed HIV replication on ART and HCV-monoinfected
- FPR accelerated among HIV viremic patients with CD4 counts < 500/mm³

Impact of ART on Survival with Decompensated Cirrhosis

• Prospective study of 153 HIV-HCV coinfected subjects with decompensated cirrhosis
• Median survival: **13 months**
• Independent predictors of mortality:

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑Child-Pugh score</td>
<td>1.22 (1.08-1.37)</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>2.45 (1.41-4.27)</td>
</tr>
<tr>
<td>CD4 count &lt;100 cells/µl</td>
<td>2.48 (1.52-4.06)</td>
</tr>
<tr>
<td>HAART during following up</td>
<td>0.57 (0.34-0.95)</td>
</tr>
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• **Cumulative 3-year survival: 18% off HAART, 40% on HAART**

Impact of HIV on HCV Disease Progression in the ART-Era

- Predicted fibrosis scores +/- HIV holding constant race, sex, alcohol use, BMI, HBsAg status, HCV RNA level
- HIV-HCV have liver fibrosis equivalent to HCV-mono 9.2 yrs older on average

Summary

• HCV coinfection is common among HIV+
  – Prevalence varies by population
  – HIV+ MSM are new high risk group

• HIV influences the natural history of HCV-related liver disease
  – Beneficial impact of potent ART
Summary

• Other modifiable risk factors include:
  – Alcohol abuse
  – Marijuana use
  – Obesity and insulin resistance