HIV and Viral Hepatitis
Brothers in Harm

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Figure 2: Leading causes of mortality and trends, 1990–2013
COPD=chronic obstructive pulmonary disease.

Stanaway JD et al The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013 Lancet
<table>
<thead>
<tr>
<th>Category</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total deaths</td>
<td>3909 (100.0)</td>
</tr>
<tr>
<td>AIDS-related</td>
<td>1123 (28.7)</td>
</tr>
<tr>
<td>Liver-related</td>
<td>515 (13.2)</td>
</tr>
<tr>
<td>- Chronic viral hepatitis</td>
<td>447 (11.4)</td>
</tr>
<tr>
<td>- Liver failure</td>
<td>68 (1.7)</td>
</tr>
<tr>
<td>CVD-related</td>
<td>436 (11.1)</td>
</tr>
<tr>
<td>- MI, definite or possible</td>
<td>225 (5.9)</td>
</tr>
<tr>
<td>- Stroke</td>
<td>56 (1.4)</td>
</tr>
<tr>
<td>- Other CVD</td>
<td>60 (1.5)</td>
</tr>
<tr>
<td>- Other heart disease</td>
<td>86 (2.2)</td>
</tr>
<tr>
<td>- Complications due to diabetes mellitus</td>
<td>9 (0.2)</td>
</tr>
<tr>
<td>Non-AIDS cancer</td>
<td>590 (15.1)</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>1245 (31.8)</td>
</tr>
<tr>
<td>- Suicide</td>
<td>150 (3.8)</td>
</tr>
<tr>
<td>- Drug overdose</td>
<td>109 (2.8)</td>
</tr>
<tr>
<td>- Euthanasia</td>
<td>16 (0.4)</td>
</tr>
<tr>
<td>- Homicide</td>
<td>22 (0.6)</td>
</tr>
<tr>
<td>- Accident</td>
<td>74 (1.9)</td>
</tr>
<tr>
<td>- Invasive bacterial infection</td>
<td>259 (6.6)</td>
</tr>
<tr>
<td>- Lactic acidosis</td>
<td>17 (0.4)</td>
</tr>
<tr>
<td>- Pancreatitis</td>
<td>20 (0.5)</td>
</tr>
<tr>
<td>- Renal dysfunction/ disease</td>
<td>48 (1.2)</td>
</tr>
<tr>
<td>- Other</td>
<td>266 (5.8)</td>
</tr>
<tr>
<td>- Unknown</td>
<td>264 (6.8)</td>
</tr>
</tbody>
</table>

*Includes liver cancers as a result of viral hepatitis-related liver failure. Includes lung cancers, prostate cancers, anal cancers, head- and neck cancers, Hodgkin’s lymphomas, primary liver cancers (excluding hepatitis-related liver cancers, which are classified as “chronic viral hepatitis”), gastrointestinal cancers, breast cancers, uterus cancers, testicular cancers, penile cancers bladder cancers, kidney cancers, primary bone tumors, brain tumors (except non-Hodgkin’s lymphomas), unknown primary tumors and acute/chronic leukemias. Most commonly reported cancers: lung (n=155), anal (38), head and neck (35), Hodgkin’s lymphoma (26).

Table 3. Results from adjusted and unadjusted Poisson regression assess the association of HIV/hepatitis co with all-cause, liver-related, and AIDS-related mortality.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hepatitis coinfection</th>
<th>Unadjusted</th>
<th>Adjusted&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk ratio (95% CI)</td>
<td>P value</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>HIV monoinfected</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>HIV/HBV coinfecte</td>
<td>1.88 (1.52–2.32)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>HIV/HCV coinfecte</td>
<td>2.29 (1.94–2.70)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>HIV/HBV/HCV triple infected</td>
<td>2.97 (2.12–4.14)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Liver-related mortality</td>
<td>HIV monoinfected</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>HIV/HBV coinfecte</td>
<td>13.21 (7.62–22.90)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>HIV/HCV coinfecte</td>
<td>12.74 (7.69–21.12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>HIV/HBV/HCV triple infected</td>
<td>23.22 (11.24–47.98)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

<sup>a</sup> Adjusted for age, sex, race, education, income, and insurance status.
Why are coinfections prevalent among PLWH?

Share the same route of transmission

Both attack same populations
HBV coinfection: Epidemiology

• Worldwide prevalence among PLWH – 3-59%

Askari A etal 2014 Prevalence of hepatitis B co-infection among HIV positive patients: narrative review article Iranian Journal of Public Health
HBsAg seropositivity among PLWH

- MSM
- Heterosexual
- IDUs
HBsAg seropositivity: Turkey

Erdinç Ş etal manuscript in preparation
HBV coinfection

Guertler LG 2014 *Effect of antiretroviral HIV therapy on hepatitis B virus replication and pathogenicity* Intervirology
HBV coinfection

- Less HBsAg and HBeAg clearance
- Bizarre HBV serology
  - HBsAg negative hepatitis
- HBV related immune activation may lead to HIV replication
- Low ALT levels
  - Elevated HBV viral load during pregnancy
- HBV related flares are common

Rajbhandari R et al 2016 *HBV/HIV coinfection is associated with poorer outcomes in hospitalized patients with HBV or HIV*. Journal of Viral Hepatitis
Boyd A et al 2019 *Effect of hepatitis B virus (HBV) surface-gene variability on markers of replication during treated human immunodeficiency virus-HBV infection in Western Africa* Liver Internat
HBV coinfection

- Accelerated cirrhosis
- Discontinuation of HBV active treatment is a disaster
- More ART related toxicity
- More decompensation
- Poorer in-hospital outcomes

Rajbhandari R et al 2016 *HBV/HIV coinfection is associated with poorer outcomes in hospitalized patients with HBV or HIV.* Journal of Viral Hepatitis
HBV coinfection

- Residual viremia is common
  - HBV DNA< 2000iu/ml, blips?

Boyd A etal 2019 Effect of hepatitis B virus (HBV) surface-gene variability on markers of replication during treated human immunodeficiency virus-HBV infection in Western Africa Liver Internat
HBV coinfection: Treatment

- All HBsAg positive patients should receive tenofovir containing ART
HBV coinfection: Treatment

Gallant J et al 2015 Efficacy and Safety of Switching to Simpler Single-Tablet Regimen of Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) in HIV-1/Hepatitis B Coinfected Adults in North America and Japan (NCT02071082): Week 48 Results 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention
HBV coinfection: Treatment

No change in HBV related adverse events in patients under tenofovir containing regimens

Peters L etal 2018 *Uptake of tenofovir-based antiretroviral therapy among HIV-HBV-coinfected patients in the EuroSIDA study* Antiviral Therapy
HBV coinfection: Follow-up

Hearn B et al. 2015 Low adherence of HIV providers to practice guidelines for hepatocellular carcinoma screening in HIV/hepatitis B coinfection. Clinical Infectious Diseases.
Hepatitis B: Gaps in knowledge

- Only 1.2% of GPs can define screening for complications
- 11% did not know HBV is carcinogenic
- 23% believe HBV may evolve to HCV
VIRAL HEPATITIS C IN THE WORLD

- 15m Eastern Mediterranean
- 14m Europe
- 10m South-East Asia
- 14m Western Pacific
- 10m Africa
- 7m Americas
- 71m Global
HCV coinfection: Epidemiology

- HIV infected 37 M
  - 2,278,400 HCV coinfected
  - 1,362,700 in PWID
  - 6.4% MSM

HCV coinfection: Epidemiology

Erdinç Ş et al. manuscript in prep
HCV coinfection

- HCV cure is an achievable goal
- Reinfection is common
  - 15 cases per 100 patient years
- Spontaneous clearance is rare
- Transmission route matters
  - Non-IVDU PLWH clear rapid
HCV coinfection: Evolution of treatment

- **1991**: Standard IFN (6 mos)
- **1998**: IFN + RBV
- **2001**: PEG-IFN
- **2011**: DAAs
- **2013**: 85% SVR
- **2016**: 95-100% SVR

*Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD.*
HCV coinfection: Treatment

- Same with monoinfected

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Pangenotypic regimens</th>
<th>Genotype-specific regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SOF/VEL</td>
<td>GLE/PIB</td>
</tr>
<tr>
<td>Genotype 1a</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Genotype 1b</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Genotype 2</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Genotype 3</td>
<td>Yes^c</td>
<td>Yes</td>
</tr>
<tr>
<td>Genotype 4</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Genotype 5</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Genotype 6</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

EASL HCV Guidelines 2018 *Journal of Hepatology*
<table>
<thead>
<tr>
<th>NRTIs</th>
<th>Abacavir</th>
<th>Emtricitabine</th>
<th>Lamivudine</th>
<th>Tenofovir disoproxil fumarate</th>
<th>Tenofovir alafenamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNRTIs</td>
<td>Efavirenz</td>
<td>Etravirine</td>
<td>Nevirapine</td>
<td>Rilpivirine</td>
<td></td>
</tr>
<tr>
<td>Protease inhibitors</td>
<td>Atazanavir/ritonavir</td>
<td>Atazanavir/cobicistat</td>
<td>Darunavir/ritonavir</td>
<td>Darunavir/cobicistat</td>
<td>Lopinavir/ritonavir</td>
</tr>
<tr>
<td>Entry/integrase inhibitors</td>
<td>Dolutegravir</td>
<td>Elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate</td>
<td>Elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide</td>
<td>Maraviroc</td>
<td>Raltegravir</td>
</tr>
</tbody>
</table>
HCV coinfection: Opportunities

- Interferon free / ribavirin free
- Genotype independent regimens
- Effective second line options
- Tolerable regimens
  - A regime suitable for your very patient
- Potent therapy = potent prevention
  - Microelimination
  - Iceland
  - Georgia
HCV coinfection: challenges

- Budget
- Finding HCV infected patients
- Retreatment
  - Treatment failure?
  - Re-infection
- Post cure follow-up is essential
To conclude

- Coinfections are common in PLWH
- Coinfections lead to mortality/morbidity in PLWH
- Lack of sterilizing HBV therapy necessitates lifelong therapy
- DAA’s pave the way to global HCV elimination
- Knowledge gap is a barrier in the care of patients