Treating coinfection in Asia: Challenges and unmet needs

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HIV/HCV coinfection: Public Health Challenges in Asia

- Prevalence, HCV genotype distribution and disease progression
- HCV treatment outcome in Asia
- Challenges in providing treatment and care
Burden of HIV/HCV in Asia

Prevalence of HIV/HCV co-infection has not been comprehensively estimated.

Very low awareness/knowledge of HCV status among several risk groups and providers.

3.5 million HIV
32 million HCV

8-10% PWID
90%

China 40-95%
Blood

% of adult population
infected with HIV
HCV prevalence in Treat Asia HIV Database (N=1469) in 2005

2979 HIV, 12 countries
49% had HCV testing
44 PWID (5%)

HCV prevalence 10.4%

March 2012, N 6,360 in TAHOD:
- 65.3% had HCV testing.
- 17.7% had positive HCV Ab.
- Only 4.4% of those had received HCV PCR testing.
- 43.8% were found to have positive HCV RNA.
- Only very few had received treatment.

Estimated 2-9 M PWID in Asia –

Underestimation of HCV coinfection and low number of PWID in HIV treatment and Care
Expensive, inadequate HCV RNA

Zhou et al. JGH 2007: 22: 1510-1518
Walsh et al. JAIDS 2007: 45: 363-365

IDU: major mode of HIV transmission in many Asian countries
Myanmar 30%, China 40%, Majority in Vietnam, Indonesia and Malaysia

Underestimation of HCV coinfection and low number of PWID in HIV treatment and Care
Expensive, inadequate HCV RNA
HCV incidence and genotype distribution in Asia

HCV GT 6 is circulating mainly in Vietnam, Thailand and southern China

Sievert et al. Liver International 2011:61-80
Favorable *IL28B* rs12979860 CC Genotype in Asia

*IL28B* polymorphisms associated with
- Higher SVR rates\(^1\)
- Higher RVR rates\(^2\)
- Higher HCV RNA\(^3\)
- Higher LDL levels\(^4\)
- Higher baseline ALT levels\(^5\)
- Higher rate of spontaneous viral clearance\(^6\)

IL-28b (rs12979860), and HCV viral load between 130HIV/HCV and 331 HCV mono, Thailand: GT3:47% ; GT1, 34% GT6:18%

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>HIV/HCV</th>
<th>HCV mono</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-28b (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.514</td>
</tr>
<tr>
<td>C/C</td>
<td>86.6</td>
<td>88.3</td>
<td>84.7</td>
<td></td>
</tr>
<tr>
<td>C/T</td>
<td>11</td>
<td>10.6</td>
<td>11.8</td>
<td></td>
</tr>
<tr>
<td>T/T</td>
<td>2.2</td>
<td>1</td>
<td>3.5</td>
<td></td>
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<tr>
<td>HCV RNA Median (IQR)</td>
<td>6.2(5.6-6.9)</td>
<td>6.7(5.6-7.3)</td>
<td>5.8(5.6, 6.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HCV RNA &gt;800,000 copies/ml</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FibroScan, PKa</td>
<td>10.5</td>
<td>8.5 (6.4-13.85)</td>
<td>6.6 (4.9-9.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;7.1 kPa, N(%)</td>
<td>220 (50.1)</td>
<td>33 (30.6)</td>
<td>187 (56.5)</td>
<td></td>
</tr>
<tr>
<td>7.2-9.4 kPa , N (%)</td>
<td>91(20.7)</td>
<td>30 (27.8)</td>
<td>61 (18.4)</td>
<td></td>
</tr>
<tr>
<td>9.5-14 kPa , N (%)</td>
<td>60 (13.8)</td>
<td>19 (17.6)</td>
<td>41 (12.4)</td>
<td></td>
</tr>
<tr>
<td>&gt;14 kPa, N(%)</td>
<td>68 (15.5)</td>
<td>26 (24.1)</td>
<td>42 (12.7)</td>
<td></td>
</tr>
</tbody>
</table>

2/3 meet criteria for treatment
1/4 require HCC screening
Multiple challenges of HIV/HCV management in Asia

Medical ineligibilities
- Substance use
- Psychiatric disorder
- Co-morbidities: TB
- Stage of liver disease

System barrier
- Lack of access to care
- Cost of drug and monitoring (HCV RNA, genotype, Liver biopsy/fibroscan)

Care provider barriers
- Failure of screening
- Adherence risk
- Side effects, drug interaction
- Social stigma
- LTFU

Patient barriers
- Refusal
# Treatment challenges: High cost of HCV treatment in Asia

<table>
<thead>
<tr>
<th>Countries</th>
<th>Anti HCV ab</th>
<th>HCV RNA USD</th>
<th>Peg IFN/RBV</th>
<th>Administrative costs</th>
<th>Total cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>$5-$10</td>
<td></td>
<td>$18,000</td>
<td>Unknown</td>
<td>$18,000</td>
</tr>
<tr>
<td>India</td>
<td>$4-$8</td>
<td>132</td>
<td>$15,000-$16,000</td>
<td>Unknown</td>
<td>$15,000-$16,000</td>
</tr>
<tr>
<td>Indonesia</td>
<td>$25-$35</td>
<td>92</td>
<td>$17,000-$18,500</td>
<td>$9,000-$11,500</td>
<td>$26,000-$30,000</td>
</tr>
<tr>
<td>Nepal</td>
<td>$2</td>
<td>126</td>
<td>Treatment not available</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Thailand</td>
<td>$6-$9</td>
<td>100-120</td>
<td>$18,000</td>
<td>$15,000</td>
<td>$33,000</td>
</tr>
<tr>
<td>Vietnam</td>
<td>$10</td>
<td></td>
<td>$12,000</td>
<td>$16,000</td>
<td>$28,000</td>
</tr>
</tbody>
</table>

Metheny, N. 2010. *Dying for Treatment: HCV Treatment Out of Reach in Asia*

Thai AIDS Treatment Action Group (TTAG)
Lack of recognition of the importance of the drugs PEG-IFN and RBV not yet on the WHO Essential Medicines List

Marginal commitment from international donors to support efforts to tackle and treat Hep C.

Country Plans, Guidelines, and Resources

Few countries have a national plan to address/treat HCV
Treatment of Chronic Hepatitis C

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Treatment regimen</th>
<th>Country</th>
<th>SVR rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1:</td>
<td>PegIFN plus SD RBV for 48 weeks</td>
<td>China¹</td>
<td>74%</td>
</tr>
<tr>
<td></td>
<td>PegIFN plus SD RBV for 48 weeks</td>
<td>Japan²</td>
<td>61%</td>
</tr>
<tr>
<td></td>
<td>PegIFN plus SD RBV for 24 weeks</td>
<td>Taiwan⁴,⁵,⁶,⁷</td>
<td>76-79%</td>
</tr>
<tr>
<td>Genotype 1, LVL, and RVR</td>
<td>PegIFN plus SD RBV for 24 weeks</td>
<td>Taiwan⁷</td>
<td>84%</td>
</tr>
<tr>
<td></td>
<td>PegIFN plus SD RBV for 24 weeks</td>
<td>Korea³</td>
<td>94%</td>
</tr>
<tr>
<td>Genotype 2/3</td>
<td>PegIFN plus SD RBV for 24 weeks</td>
<td>Taiwan⁸</td>
<td>95%</td>
</tr>
<tr>
<td>Genotype 2/3 and RVR</td>
<td>PegIFN plus SD RBV for 16 weeks</td>
<td>Taiwan⁸</td>
<td>100%</td>
</tr>
<tr>
<td>Genotype 4</td>
<td>PegIFN plus SD RBV for 48 weeks</td>
<td>Kuwait⁹</td>
<td>68%</td>
</tr>
<tr>
<td>Genotype 6</td>
<td>PegIFN plus SD RBV for 48 weeks</td>
<td>Hong Kong¹⁰</td>
<td>86%</td>
</tr>
</tbody>
</table>


Peg IFN/RBV remains a standard of care for GT 1 in Asia¹¹
High SVR rates in Asian HCV infection
Korea: High SVR rates in HCV GT1 with Peg/RBV in clinical practice

272 HCV
Clinical trial group n=51 (GT1=26; cirrhosis 7.7% GT1)
Clinical practice n=221 (GT1=106, cirrhosis 21.7% each)
Peg alfa2a/RBV, 24 weeks for GT2

Non adherence (n=68: 25%)
- lab abnormal : 70% anemia, 35% neutropenia
- Adverse symptoms: 54%

1Heo NY CMH 2013:19:60-69
Factors contributing to SVR rates in HIV/HCV in Asia

- HIV-related immune suppression
  - Advanced HIV
- More advanced liver fibrosis\(^1\)
  - Insulin resistance\(^2;3\)
  - Genotype\(^3\)\(^4\)
- Higher HCV RNA
- Higher treatment discontinuation
  - Toxicity: anemia, low body weight, mitochondrial toxicity
- Lower RBV dosing (800 mg vs 1000/1200 mg daily)
- Drug interaction

\(^1\) Avihingsanon et al. APASL 2013
\(^2\) Patel et al. JGH 2011:26:1182
\(^3\) Hull et al. AIDS:26:1789
\(^4\) Barreiro P CID 2006: 42:1032
\(^5\) APASL consensus statement Hepatol Int 2012:6:409
HCV treatment in HIV infected patients in developed countries is well established

**But**

there is limited data in Asia
Effectiveness and Tolerability of Hepatitis C Treatment in HIV Co-infected Patients in Routine Care Services in Asia: A Pilot Model of Care Project

4 sites: Indonesia, Thailand, Vietnam, Malaysia.

Up to 400 HIV-infected patients under care (100 per site), and with known HCV Ab, will receive HCV-RNA testing.

Those with confirmed chronic infection will receive:

- HCV genotyping
- IL28B testing,
- Liver fibrosis assessment with Fibroscan.

- 200 patients (50 per site) with treatment indication will be offered treatment with Pegylated-interferon and Ribavirin
All genotypes
Sub-study
Ribavirin PK
(Thailand)
Challenges of Using Protease Inhibitors (Telaprevir: TPV; Boceprevir: BOC) in clinical practice

- Pill burden
  - BOC 4 X 200 mg 8 hourly = 12 capsules / day
  - TPV 2 X 375 mg 8 hourly = 6 tablets /day (9 if EFV)

- Need to have with food
  - TPV with 20g fat to increase absorption
  - BOC with food
  - Some HIV drugs have food restrictions (e.g. EFV needs to be taken in fasting state)

- Take with RBV (5-6 tablets/day)

- If HIV and on ART, further pill burden

- Potential issues of adherence

- Expensive

- Drug interaction with ARV and others (CYP450)

- Increase in adverse effects
  - TPV: anemia, rash
  - BOC: anemia, dysguesia

- Concerns over resistance
Thailand: Free HCV treatment (Peg IFN/RBV) for GT2/3

- Diagnostic and treatment monitoring costs are not covered.
- only 24 weeks of Peg IFN/RBV is provided (HIV-HCV requires 48 weeks
- Reimbursement criteria are as follows:
  - 18-65 years of age;
  - HCV genotype 2&3 only;
  - ALT ≥ 1.5 x;
  - HCV RNA ≥ 5,000 UI/ml;
  - Liver biopsy metavir score ≥ 2 or fibroscan pKa≥7.5.
- Funding coverage is needed for drugs, patient support, monitoring, and treatment complication

<table>
<thead>
<tr>
<th>Countries</th>
<th>Population</th>
<th>HCV estimates</th>
<th>Cases treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taiwan</td>
<td>23 M</td>
<td>490,000</td>
<td>9,000</td>
</tr>
<tr>
<td>Thailand</td>
<td>67 M</td>
<td>1,200,000</td>
<td>3,000</td>
</tr>
<tr>
<td>Malaysia</td>
<td>30 M</td>
<td>30,000</td>
<td>1,000</td>
</tr>
<tr>
<td>Vietnam</td>
<td>90 M</td>
<td>1,800,000</td>
<td>1,500</td>
</tr>
<tr>
<td>Myanmar</td>
<td>49 M</td>
<td>1,000,000</td>
<td>500</td>
</tr>
<tr>
<td>India</td>
<td>1,100 M</td>
<td>10,000,000</td>
<td>8,000</td>
</tr>
</tbody>
</table>

Source: MSD
Conclusion: strategies to reduce disease burden of HIV/HCV coinfection in Asia

- Awareness and education program on HCV
- Facilitate integration of HCV-related services into routine HIV care settings
- Harm reduction strategies for PWID
- HCV screening in high risk population: PWID, MSM, sex worker, blood transfusion
- Regular HCV screening for HIV-infected MSM, PWID
- Improved access to ART and initiation ART earlier
- Enhanced liver disease staging (ie Fibroscan)
- Promote HCV treatment and care: treatment as prevention
- IFN-free HCV treatment regimens
HCV is curable

It is absolutely impossible to put a price on the patient’s quality of life as it is priceless and invaluable.
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