HIV and Co-infections

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  – Abbott Diagnostics
HIV and Co-infections

TB

HCV

STIs

HBV
WHO Hepatitis 2030 Elimination Targets

**PREVENTION**
- 90% coverage of 3-dose HBV vaccine for infants
- 90% cases of mother-to-child transmission of HBV prevented
- 100% of blood donations screened & 90% of medical injections safe
- 300 sterile syringes distributed per year to each PWID

**TREATMENT**
- 90% of those infected diagnosed and 80% of those eligible treated

**SERVICE COVERAGE TARGETS**

**IMPACT LEADING TO ELIMINATION**
- 90% reduction in incidence of chronic HBV and HCV infection
- 65% reduction in mortality to chronic HBV and HCV

*Estimated 7.1 million deaths averted*
HBV Global Scenario (HBsAg)

Global Prevalence: 3.9% translating about 291 million HBsAg positive persons globally

India prevalence: 2.5% translating to about 33 million HBsAg infections

Razavi-Shearer D et al; Lancet Gastroenterol Hepatol 2018
Global Prevalence: 1.0% translating about 61 million HCV RNA+ persons globally

India Prevalence: 0.5% translating to about 6.2 million HCV chronic infections
HIV/Viral Hepatitis Co-infection

- **2 - 4** million persons coinfected with HIV/HBV (~10% of all HIV-infected)
- **2 - 10** million persons coinfected with HIV/HCV (~30% of all HIV-infected)

Basnayake et al; J Vir Hepatitis 2016
HCV and HIV/HCV epidemics among PWID in India

Solomon SS et al, Lancet ID 2015
## HIV, HBV & HCV: Similarities and Differences

<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>HBV</th>
<th>HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectiousness</strong></td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Spontaneous clearance</strong></td>
<td>-</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Modes of transmission</strong></td>
<td>• Sexual</td>
<td>• Sexual</td>
<td>• Parenteral</td>
</tr>
<tr>
<td></td>
<td>• Parenteral</td>
<td>• Parenteral</td>
<td>• Blood and blood products</td>
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<td>• Blood and blood products</td>
<td>• Blood and blood products</td>
<td>• Vertical transmission</td>
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<td>• Vertical transmission</td>
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</tr>
<tr>
<td><strong>Suppressive therapy</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>-</td>
</tr>
<tr>
<td><strong>Curative therapy</strong></td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Vaccine</strong></td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
The natural history of HBV

- HBV infection
- Chronic Infection: 5-95%
  - Resolved
  - Cirrhosis: ~20-30%
    - “Healthy carrier”
  - Liver failure or cancer: 8%/yr
- Progression accelerated with age, alcohol, aflatoxin

20 years

(Family Planning Association of India)
HIV impacts the natural history of HBV....

- **HIV increases the frequency of HBV viral persistence**
  - ~5% in HBV mono-infected adults

**Table 1:** HBV markers and rate of chronic HBV infection in HIV-1 infected patients grouped according to risk factor

<table>
<thead>
<tr>
<th>HBV markers</th>
<th>Rate of chronic HBV infection (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sAg+</td>
<td>25</td>
</tr>
<tr>
<td>sAg-</td>
<td>75</td>
</tr>
<tr>
<td>sAb-</td>
<td>40</td>
</tr>
<tr>
<td>sAb+</td>
<td>8%</td>
</tr>
<tr>
<td>sAb-</td>
<td>95%</td>
</tr>
</tbody>
</table>

- **HIV is also associated with....**
  - Higher HBV DNA levels
  - Accelerated loss of protective anti-HBs antibodies
  - Reactivation of HBV in “Healthy carriers”

...and accelerates HBV disease progression

- Multicenter AIDS cohort study
- 5293 men (326 HBsAg+ baseline)

**Flowchart**

1. **HBV infection**
2. **Chronic Infection** → 5-95% → **Resolved**
3. **Cirrhosis** → ~20-30%
4. **Liver failure or cancer** → 8%/yr

20 years (progression accelerated with age, alcohol, aflatoxin)

Liver MR/1000 PYs

- HIV+/HbsAg-
- HIV+/HbsAg+
- HIV+/HbsAg-
- HIV+/HbsAg+

Thio et al; Lancet 2002
Natural History of HCV

HCV infection

Resolved

Chronic Infection
75-85%

Stable

Cirrhosis
~20%

Compensated

Liver failure or cancer
4-6%/yr

(Progression accelerated with age, alcohol, aflatoxin)

Thomas DL 1995; Poynard 1997; Thomas 2000
HIV increases HCV viral load and persistence

- Frequency of HCV viral persistence ~10% higher in HIV+ vs. HIV-
- Data from the ALIVE Study

- **Resolved**
- **Chronic Infection**
  - 75-85%
  - ~20%
- **Cirrhosis**
  - 4-6%/yr
- **Liver failure or cancer**

20 years (progression accelerated with age, alcohol, aflatoxin)

Thomas DL 1995; Poynard 1997; Thomas 2000
HIV increases risk of cirrhosis

20 years
(progression accelerated with age, alcohol, aflatoxin)

HCV infection

- 75-85%

Chronic Infection

- ~20%

Resolved

Stable

Cirrhosis

- 4-6%/yr

Compensated

Liver failure or cancer

Risk ratios of cirrhosis individuals with HIV/HCV co-infection compared with HCV mono-infection

Thein et al; AIDS 2008
HIV increases risk of liver failure

- HCV infection
  - 75-85%
  - Chronic Infection
    - ~20%
    - Cirrhosis
      - 4-6%/yr
      - Liver failure or cancer

Data from the multicenter hemophilia cohort

Non-hepatic deaths in HIV+
Liver failure in HIV+
Liver failure in HIV-

20 years (progression accelerated with age, alcohol, aflatoxin)

Thomas JAMA 2000; Thomas JID 1996; Benhamou Hepatology 1999; Goedert Blood 2002
Advance in HCV therapeutics

- IFN
- IFN + RBV
- PEG + RBV
- BOC/TPV+PEG+RBV
- New DAA + PEG + RBV
- IFN Free
- IFN/RBV free

Global progress towards elimination

HBV continuum of care by WHO region, 2016

HCV continuum of care by WHO region, 2016
HCV care cascade among PWID in India

- Primary reason for not being tested was **never having heard** of hepatitis C (n=6,138 [50%])
- Primary reason for not being tested among those who had heard of hepatitis C was **low perceived risk** (73%)

5,777 HCV-infected PWID from 15 cities across India (community-based sample)

Solomon SS et al, Lancet ID 2015
India’s plan for viral hepatitis

1. Combat hepatitis and achieve country wide elimination of hepatitis C by 2030

2. Achieve significant reduction in the infected population, morbidity and mortality associated with hepatitis B and C virus viz. cirrhosis and hepatocellular carcinoma (liver cancer)

3. Reduce the risk, morbidity and mortality due to hepatitis A and E
Components of the plan

1. Enhance community awareness on hepatitis and lay stress on preventive measures among general population especially high risk groups and in hotspots

2. Provide early diagnosis and management of viral hepatitis at all levels of healthcare

3. Develop standard diagnostic and treatment protocols for management of viral hepatitis and its complications

4. Strengthen the existing infrastructure facilities, build capacities of existing human resources and raise additional human resources where required or providing comprehensive services for management of viral hepatitis and its complications in all districts of the country

5. Develop linkages with existing national programmes towards awareness, prevention, diagnosis and treatment of viral hepatitis

6. Develop a web-based ‘Viral Hepatitis Information Management System’ to maintain a registry of persons affected with viral hepatitis and its sequelae
Opportunities for Integration

- Integrating screening for HIV and viral hepatitis
RDS in Kanpur
RDS in Kanpur
RDS in Kanpur
RDS in Kanpur

HIV/HCV negative

HIV & HCV positive

HIV only
RDS in Kanpur
RDS in Kanpur
RDS in Kanpur
RDS in Kanpur
RDS in Kanpur

- HIV/HCV negative
- HIV & HCV positive
- HIV only
RDS in Kanpur

HIV Prevalence: 31%
Unaware of HIV status: 97.2%
HCV Prevalence: 65%
Unaware of HCV status: 100%
Cost of RDS to identify HCV infections

If integrated with HIV, it would only cost an additional USD 10 to find one HCV unaware PWID!

Solomon SS et al, PLOS Medicine 2017
Opportunities for Integration (Diagnosis)

- Integrating screening for HIV and viral hepatitis
- Integration with HIV and harm-reduction services
Integrating HIV with HCV, TB MAT and SSP: An example from India

**TB Testing & Treatment**
Symptom screen and sputum collection on-site; Testing and treatment from DMC/DOTS centers

**General medical care:** Glucose screening, blood pressure monitoring, doctor available for general health problems

**HCT:** rapid testing performed on-site; positive results confirmed at govt center

**Syringe services**
Field-based & on-site

**STI syndromic management**
Government sponsored

**Condoms**

**Counseling:** Individual & group/substance use, alcohol, adherence, couples, family etc

**ART:** delivered through a link model (ARVs provided by government but peer health worker picks up meds so clients can receive directly from ICC)

**HCV testing:** Rapid on-site HCV testing
Impact of integrating HIV and HCV

- **Significant impact** on community HCV testing and awareness
- **Modest impact** on linkage to HCV care, treatment uptake, cure
- Need on-site HCV treatment, other strategies (peers, incentives) for linkage

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Adjusted Prevalence Ratio (aPR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV testing, ever</td>
<td>0.2, 1.34, 3.69, 10.2</td>
</tr>
<tr>
<td>Aware of status, HCV Ab+</td>
<td>0.87, 1.14, 3.69, 7.11</td>
</tr>
<tr>
<td>Linkage to care, HCV RNA+</td>
<td>0.87, 1.52, 5.36, 3.69</td>
</tr>
<tr>
<td>Initiated treatment, HCV RNA+</td>
<td>1.52, 6.02, 9.86, 36.7</td>
</tr>
<tr>
<td>Achieved SVR, among treated</td>
<td>0.78, 1.52, 5.36, 36.7</td>
</tr>
</tbody>
</table>
HIV and Co-infections/Comorbidities

- TB
- HCV
- STIs
- HBV
- Mental health issues
### Depression, alcohol and substance use

#### Predictors of viral suppression in a sample of 1454 ART eligible MSM in India

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PR</th>
<th>(95% CI)</th>
<th>aPR</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol dependence</td>
<td>0.58</td>
<td>(0.44–0.78)</td>
<td>0.71</td>
<td>(.53–.95)</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.90</td>
<td>(0.65–1.26)</td>
<td>0.86</td>
<td>(.64–1.15)</td>
</tr>
<tr>
<td>Recreational drug use</td>
<td>0.59</td>
<td>(0.33–1.06)</td>
<td>0.64</td>
<td>(.40–1.02)</td>
</tr>
</tbody>
</table>

#### Among those with alcohol dependence

<table>
<thead>
<tr>
<th></th>
<th>Ref</th>
<th>(95% CI)</th>
<th>Ref</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neither</td>
<td></td>
<td>...</td>
<td></td>
<td>...</td>
</tr>
<tr>
<td>Severe depression</td>
<td>1.27</td>
<td>(1.11–1.46)</td>
<td>1.03</td>
<td>(.88–1.21)</td>
</tr>
<tr>
<td>Recreational drug use</td>
<td>0.42</td>
<td>(.14–1.22)</td>
<td>0.45</td>
<td>(.20–.99)</td>
</tr>
<tr>
<td>Both severe depression and recreational drug use</td>
<td>0.23</td>
<td>(.09–.59)</td>
<td>0.23</td>
<td>(.09–.57)</td>
</tr>
</tbody>
</table>

*P* value for interaction < .01  ...

#### Three-way interaction between alcohol, depression and substance use among MSM in India

Prabhu S et al; Clinical Infect Dis 2019
The goal of HIV programs should be to treat the INDIVIDUAL as a WHOLE and not individual diseases/co-infections.
Acknowledgements

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  - Elton Johns AIDS Foundation
  - Abbott Diagnostics