HIV in Indonesia: Clinical Challenges

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Head of Tropical – Infectious Disease
Fac of Medicine - UGM
Outline

• HIV in Indonesia –
  – The 2015 IBBS (Integrated Biology and Behaviour Survey)
  – The HIV & AIDS cases, test, treatment
  – Cohort of the impact of Antiretroviral Therapy
  – HIV in Dr. Sardjito Hospitals

• Clinical problems on HIV
  – TB-HIV
  – Hepatitis – HIV
  – Drug toxicities
  – Mortality

• Closing - opportunities
Foreword

• Indonesia is one of the countries who did not meet the MDG target
• The first case was found in 1987
• The effort to fight against HIV started 1994 and then continued to a national action starting 2004
• The country is so big with different epidemic, in scale and type
Epidemic Situation – Result of 2015 IBBS (Integrated Biological & Behavioral Survey)

• 11 (out of 34) Provinces, 22 (out of 509) Districts / Cities
• Survey Population:
  – Direct Sex Worker
  – Indirect Sex Worker
  – Fishermen (those working in the ships)
  – Truck drivers, Taxi-motor driver, Public transport drivers
  – Injecting-drug users
  – Transgender
  – Man having sex with man (MSM)
  – Prisoners
  – Youth and Adolescents
**IBBS Sites**

<table>
<thead>
<tr>
<th>No</th>
<th>Province</th>
<th>Districts/Cities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>North Sumatra</td>
<td>Medan, Deli Serdang, Serdang Begadai</td>
</tr>
<tr>
<td>2</td>
<td>Riau Island</td>
<td>Batam</td>
</tr>
<tr>
<td>3</td>
<td>Jakarta Special Province</td>
<td>North Jakarta, Central Jakarta, West Jakarta, South Jakarta, East Jakarta</td>
</tr>
<tr>
<td>4</td>
<td>West Java</td>
<td>Bandung, Bekasi and the region</td>
</tr>
<tr>
<td>5</td>
<td>Central Java</td>
<td>Semarang, Batang</td>
</tr>
<tr>
<td>6</td>
<td>East Java</td>
<td>Surabaya, Banyuwangi, Malang City and Malang District</td>
</tr>
<tr>
<td>7</td>
<td>Bali</td>
<td>Denpasar</td>
</tr>
<tr>
<td>8</td>
<td>East Nusa Tenggara</td>
<td>Kupang</td>
</tr>
<tr>
<td>9</td>
<td>Papua</td>
<td>Jayapura and the region</td>
</tr>
<tr>
<td>10</td>
<td>Lampung</td>
<td>Bandar Lampung and the region</td>
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<tr>
<td>11</td>
<td>Maluku</td>
<td>AMbon</td>
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</tbody>
</table>
### HIV Prevalence based on Risk Groups
IBBS 2007, 2011 and 2015

#### Above 20%:
- Transgender
- MSM
- IVDU

<table>
<thead>
<tr>
<th></th>
<th>WPSL</th>
<th>WPSTL</th>
<th>Pria Risti</th>
<th>Waria</th>
<th>LSL</th>
<th>Penasun</th>
<th>WBP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2007</strong>*</td>
<td>10.00%</td>
<td>4.50%</td>
<td>0.80%</td>
<td>24.33%</td>
<td>5.33%</td>
<td>52.40%</td>
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</tr>
<tr>
<td><strong>2011</strong>*</td>
<td>10.41%</td>
<td>2.89%</td>
<td>0.70%</td>
<td>21.85%</td>
<td>8.48%</td>
<td>41.20%</td>
<td>2.95%</td>
</tr>
<tr>
<td><strong>2015</strong></td>
<td>7.97%</td>
<td>2.20%</td>
<td>0.82%</td>
<td>24.82%</td>
<td>25.80%</td>
<td>28.78%</td>
<td>2.95%</td>
</tr>
</tbody>
</table>
Siphylis Prevalence based on Risk Groups
IBBS 2007, 2011 and 2015

<table>
<thead>
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<th>WPSL</th>
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<tbody>
<tr>
<td>2007*</td>
<td>15.00%</td>
<td>6.00%</td>
<td>6.20%</td>
<td>26.67%</td>
<td>4.33%</td>
<td>1.20%</td>
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<tr>
<td>2011</td>
<td>10.16%</td>
<td>3.14%</td>
<td>4.35%</td>
<td>25.25%</td>
<td>9.29%</td>
<td>2.11%</td>
<td>4.75%</td>
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<tr>
<td>2015</td>
<td>6.49%</td>
<td>2.16%</td>
<td>2.69%</td>
<td>17.39%</td>
<td>15.71%</td>
<td>1.46%</td>
<td>2.10%</td>
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Still high: Transgender, MSM, Direct Sex Workers
Gonorrhea Prevalence based on risk group 2007, 2011 and 2015

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<th>LSL</th>
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</thead>
<tbody>
<tr>
<td>2007</td>
<td>32.00%</td>
<td>14.17%</td>
<td>28.67%</td>
<td>19.67%</td>
</tr>
<tr>
<td>2011</td>
<td>37.81%</td>
<td>18.66%</td>
<td>28.76%</td>
<td>20.80%</td>
</tr>
<tr>
<td>2015</td>
<td>21.20%</td>
<td>9.67%</td>
<td>12.22%</td>
<td>12.72%</td>
</tr>
</tbody>
</table>

Above 20%: Direct SW
## Chlamydia Prevalence based on Risk Group 2007, 2011 and 2015

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<tr>
<th></th>
<th>WPSL</th>
<th>WPSTL</th>
<th>Waria</th>
<th>LSL</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>35.00%</td>
<td>28.67%</td>
<td>29.67%</td>
<td>23.67%</td>
</tr>
<tr>
<td>2011</td>
<td>40.68%</td>
<td>40.57%</td>
<td>28.29%</td>
<td>20.53%</td>
</tr>
<tr>
<td>2015</td>
<td>32.28%</td>
<td>30.29%</td>
<td>16.78%</td>
<td>18.53%</td>
</tr>
</tbody>
</table>

Above 15%:
- Direct SW
- Indirect Sw
- Transgender
- MSM
National HIV - STI Situation

• HIV cases
  – New cases April – June 2016: 10,701 cases
  – Total until June 2016: 208,920
  – 70% are aged 25 – 49 y.o.
  – Heterosexual risk (39%), MSM (37%)

• AIDS cases
  – New cases April – June 2016: 2,962
  – Total until June 2016: 82,556
  – 37% age 30 – 39 y.o.
  – Heterosexual risk 73.8%, MSM (10.5%)

• Body Discharge 2,432 cases; Genital Ulcers 2,432 cases
HIV Services & Guideline

- HIV Test & Counseling service: 2,681
- HIV Care & Treatment: 665
- Methadone service: 92
- Sexually-transmitted infection (STI) service: 1,574
- Prevention of HIV from Mother to Child Transmission (PMTCT) services: 238 (out of \( \pm \) 1000 hospitals)
Antiretroviral Treatment (ART)

• 2 NRTI + 1 NNRTI
  – Tenofovir + Lamivudine (Emtricitabine) + Efavirenz (or Nevirapine)
  – Zidovudine Lamivudine (Emtricitabine) + Efavirenz (or Nevirapine)

• Until June 2016 People on ART : 69,954
  – 76.39% (53,433 people) on first line (NNRTI-based)
  – 20.62% (14,427 people) have ever substitute the NNRTI drug
  – 2.99% (2,094 people) on 2nd line (PI-based)
Cascade of care

- Entering HIV Care = 217,631
- Fulfill ART criteria = 164,155
- Ever receive ARV = 134,302
- Not fulfill ART criteria = 53,476
- Not yet receiving ARV = 29,853
- Transfer Out = 12,622
- Stop = 2,802
- Die = 21,115
- Still receive ARV = 69,954
- Loss to follow up = 27,809
- Transfer Out = 12,622
- Still on 1st Line = 53,433
- Substitute = 14,427
- Switch = 2,094

Locally Rooted, Globally Respected
Proportion of PLHIV still alive within 12 months on ART

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<tr>
<td>Ori</td>
<td>100.0</td>
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<td>100.0</td>
<td>100.0</td>
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<td>100.0</td>
<td>100.0</td>
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<tr>
<td>6bln</td>
<td>81.4</td>
<td>69.4</td>
<td>67.6</td>
<td>70.9</td>
<td>72.9</td>
<td>74.1</td>
<td>75.3</td>
<td>72.8</td>
<td>75.7</td>
<td>75.9</td>
<td>77.9</td>
<td>78.7</td>
<td>91.1</td>
</tr>
<tr>
<td>12bln</td>
<td>71.9</td>
<td>61.1</td>
<td>59.0</td>
<td>62.2</td>
<td>65.0</td>
<td>65.3</td>
<td>69.3</td>
<td>67.7</td>
<td>70.4</td>
<td>70.5</td>
<td>72.9</td>
<td>72.9</td>
<td>72.9</td>
</tr>
</tbody>
</table>
Proportion of mortality within 12 months of therapy

<table>
<thead>
<tr>
<th>Year</th>
<th>Proportion</th>
</tr>
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<tbody>
<tr>
<td>2004</td>
<td>25.9</td>
</tr>
<tr>
<td>2005</td>
<td>26.4</td>
</tr>
<tr>
<td>2006</td>
<td>24.9</td>
</tr>
<tr>
<td>2007</td>
<td>17.4</td>
</tr>
<tr>
<td>2008</td>
<td>17.1</td>
</tr>
<tr>
<td>2009</td>
<td>15.8</td>
</tr>
<tr>
<td>2010</td>
<td>15.6</td>
</tr>
<tr>
<td>2011</td>
<td>14.8</td>
</tr>
<tr>
<td>2012</td>
<td>12.7</td>
</tr>
<tr>
<td>2013</td>
<td>10.3</td>
</tr>
<tr>
<td>2014</td>
<td>5.7</td>
</tr>
</tbody>
</table>
Clinical Problems

• TB – HIV coinfection
• Hepatitis – HIV Coinfections
• Drug Toxicities
• Mortality
• others
Patients diagnosed as HIV infection 2013 – 2015 at Edelweis Clinic

<table>
<thead>
<tr>
<th>Month</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
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<tbody>
<tr>
<td>januari</td>
<td>927</td>
<td>1177</td>
<td>1483</td>
</tr>
<tr>
<td>Februari</td>
<td>398</td>
<td>1200</td>
<td>1518</td>
</tr>
<tr>
<td>Maret</td>
<td>951</td>
<td>1227</td>
<td>1542</td>
</tr>
<tr>
<td>April</td>
<td>979</td>
<td>1250</td>
<td>1571</td>
</tr>
<tr>
<td>Mei</td>
<td>999</td>
<td>1276</td>
<td>1592</td>
</tr>
<tr>
<td>Juni</td>
<td>1032</td>
<td>1295</td>
<td>1614</td>
</tr>
<tr>
<td>Juli</td>
<td>1060</td>
<td>1314</td>
<td>1636</td>
</tr>
<tr>
<td>Agustus</td>
<td>1070</td>
<td>1335</td>
<td>1654</td>
</tr>
<tr>
<td>September</td>
<td>1087</td>
<td>0</td>
<td>1688</td>
</tr>
<tr>
<td>Oktober</td>
<td>1115</td>
<td>1404</td>
<td>1712</td>
</tr>
<tr>
<td>November</td>
<td>1141</td>
<td>1421</td>
<td>1733</td>
</tr>
<tr>
<td>Desember</td>
<td>1158</td>
<td>1455</td>
<td>1766</td>
</tr>
</tbody>
</table>
Cumulative number of patients on ART 2013 – 2015 (subtracted by death, loss to follow ups, transfer out)

- 2013: 520
- 2014: 558
- 2015: 766
TB- HIV Coinfection

• It is a “fuel and fire” phenomena
• Prevalence of HIV (screening) among TB patients was 2%
• 60-70% of HIV patients presents as TB
• National data: Until Dec 2015 cumulative number of TB-HIV is 44,720
• Problems in clinical management:
  – Diagnosis of TB among HIV
  – Anti-TB and Anti-retroviral Therapy
  – Overlapping toxicities among Anti-TB and ARV
Several Cases TB-HIV
Hepatitis – HIV Coinfection

Clinical and Virological Characteristics of Hepatitis B or C Virus Co-Infection With HIV in Indonesian Patients

Nungkin Anggorowati,1,2 Yoshihiko Yano,1,4 Didik Setyo Heriyanto,1,2 Hanggoro Tri Rinonce,1,2 Takako Utsumi,1,2 Deshinta Putri Mulya,4 Yanri Wijayanti Subronto,4 and Yoshitake Hayashi1

1Center for Infectious Diseases, Graduate School of Medicine, Kobe University, Kobe, Japan
2Department of Anatomical Pathology, Faculty of Medicine, Dr. Sardjito Hospital, Gadjah Mada University, Yogyakarta, Indonesia
3Indonesia-Japan Collaborative Research Centre for Emerging and Re-emerging Infectious Diseases, Institute of Tropical Disease, Airlangga University, Surabaya, Indonesia
4Department of Internal Medicine, Faculty of Medicine, Dr. Sardjito Hospital, Gadjah Mada University, Yogyakarta, Indonesia

- 126 HIV patients on ART at Dr. Sardjito Hospital
- Triple infection: 4.8%
- HIV/HCV : 34.1%
- HIV/HBV : 3.2%
- Monoinfection: 57.9%
- Risk factor for HCV/HIV: IVDU
GB Virus C infection in HIV patients

GB virus C infection in Indonesian HIV-positive patients

Nungki Anggorowati¹,², Yoshihiko Yano¹,³, Yanri Wijayanti Subronto⁴, Takako Utsumi¹,⁵, Didik Setyo Heriyanto¹,², Deshinta Putri Mulya⁴, Hanggoro Tri Rinonce¹,², Dewiyani Indah Widasari¹,², Maria Inge Lusida⁵, Soetjipto⁵ and Yoshitake Hayashi¹

- GB Virus C – formerly known as hepatitis G virus (HGV) is flaviviridae family that is structurally and epidemiologically closest to Hepatitis C Virus (HCV). More prevalent in anti-HCV positive than negative → same transmission method

- The prevalence of GBV-C among HIV patients (n=125, median age 31 years) was 111/125 (88.8%), including 39/48 (81.3%) and 72/77 (93.5%) HIV infected patients with and without HCV infection, respectively.

- GBV-C isolates were of genotype 2a, 3 and 6 in 58.3%, 12.6%, and 28.4% of patients
Nevirapine substitution
(62 or 17% out of 362 pts)

incidence rate: 5 per 1000 persons per year

median time (IQR) : 8 weeks (4-17 weeks)

Risk factors associated with NVP substitution: CD4 <50 cells/mm3 and Clinical stage of 2, 3 and 4
Skin Disorders in HIV-infected Patients from West Java

*Reiva Farah Dwiyania*, Rasmia Rowawi*, Mery Lestari**, Bachti Alisjahbana***, A.J.A.M van der Ven****, Tony S. Djakakusumah*

### Table 2. Drug Eruptions Related to ARV Treatment and Suspected Drugs

<table>
<thead>
<tr>
<th>Suspected drugs</th>
<th>Total drug eruption (n=37)</th>
<th>Severe drug eruption (n=7)</th>
<th>No rash (N=806)</th>
<th>Total patients (N=843)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVP</td>
<td>23 (62.1)</td>
<td>5 (71.4)</td>
<td>335</td>
<td>358</td>
</tr>
<tr>
<td>EFV</td>
<td>4 (10.8)</td>
<td>1 (14.3)</td>
<td>186</td>
<td>190</td>
</tr>
<tr>
<td>ATD</td>
<td>3 (8.1)</td>
<td>0</td>
<td>156</td>
<td>159</td>
</tr>
<tr>
<td>CMX</td>
<td>3 (5.4)</td>
<td>1 (14.3)</td>
<td>376</td>
<td>379</td>
</tr>
<tr>
<td>Others</td>
<td>2 (5.4)</td>
<td>0</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (5.4)</td>
<td>0</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

*no data on the total patient receiving this drugs

NVP = nevirapine, EFV = efavirenz, ATD = antituberculous drugs, CMX = co-trimoxazole

Relative risk (RR) NVP versus CMX for total drug eruption: 8.1; CI: 2.4-26.8

RR EFV versus CMX for total drug eruption: 2.6; CI: 0.6-11.8

RR ATD versus CMX for total drug eruption: 2.4; CI: 0.5 - 11.7

RR NVP versus EFV for total drug eruption: 3.0; CI: 1.1-8.7

RR NVP versus EFV for severe drug eruption: 2.6; CI: 0.3-22.5
2 years Mortality
(86 out of 524 pts of 2008 – 2012)

Mortality 12.6 per 100 person-year
Highest in first 3 months of treatment
Risk factor related to mortality:
  - High clinical stage
  - TB-HIV coinfection
  - Low CD4 at time of treatment
  - Low Hb (11 gr/dl)
Other clinical problems

Incidence of syphilis seroconversion among HIV-infected persons in Asia: results from the TREAT Asia HIV Observational Database

Jin Young Ahn\textsuperscript{1,3}, David Boettiger\textsuperscript{4}, Sasisopin Kiertiburanakul\textsuperscript{5}, Tuti Parwati Merati\textsuperscript{6}, Bui Vu Huy\textsuperscript{7}, Wing Wai Wong\textsuperscript{8}, Rossana Ditangco\textsuperscript{9}, Man Po Lee\textsuperscript{10}, Shinichi Oka\textsuperscript{11}, Nicolas Durier\textsuperscript{12} and Jun Yong Choi\textsuperscript{6,12}, on behalf of the TREAT Asia HIV Observational Database\textsuperscript{1}

- The incidence of syphilis seroconversion was 5.38/100 person-years
- Incidence was higher in MSM than non-MSM (7.64 vs 2.44 / 100 py)
Neuro – AIDS : CMV, Toxo, TB, abcess
Indonesia, since 2103, started using Tenofovir as the (first) option of ARV as it can be prepared as Fixed-Dose Combination once daily.

Among 2,425 patients who received TDF, S-Cr monitoring rates increased from 1.01 to 1.84 per person per year after starting TDF (incidence rate ratio 1.68, 95%CI 1.62–1.74, p <0.001). Renal dysfunction on TDF occurred in 103 patients over 5,368 person-years of TDF use (4.2%; incidence 1.75 per 100 person-years). Risk factors for developing renal dysfunction included older age (>50 vs. ≤30, hazard ratio [HR] 5.39, 95%CI 2.52–11.50, p <0.001; and using PI-based regimen (HR 1.93, 95%CI 1.22–3.07, p = 0.005). Having an eGFR prior to TDF (pre-TDF eGFR) of ≥60 ml/min/1.73m² showed a protective effect (HR 0.38, 95%CI, 0.17–0.85, p = 0.018).
Conclusion

- HIV is still leaves clinical problems, which may lead to public health problems in Indonesia, despite the decreased number of mortality → one of which is HATI study
- Many of the problem is due to late presentation to the service
- Needed to resolve:
  - High loss to follow up
  - Tuberculosis – HIV Coinfection
  - Hepatitis – HIV Coinfection
  - STI - HIV
  - (Long-term) side effect of Antiretroviral Therapy
Opportunities

• With the increasing number of patients, we need to develop patient cohort → INDONESIA HIV OBSERVATIONAL DATA

• Need to have early detection in people who have risk → HATI Study

• Increase clinical management → TB-HIV, Hepatitis – HIV, STI – HIV, coinfection with other viruses, Toxoplasmosis in HIV, CMV in HIV, ART long-term monitoring

• Increase research capacity → continue Field Research Training Program (Collaboration with The Kirby Institute since 2009)
Field Research Training Program

- 25 Indonesian graduates
- > 30 international conference presentations
- 5 FRTP graduates have completed or are currently completing PhD studies abroad
- 5 trainees returned as mentors
- Improved written and spoken English skills
- Regional collaboration and networking
THANK YOU