Mycobacterium tuberculosis Beijing genotype is an independent risk factor for tuberculosis treatment failure in Indonesia

Ida Parwati
Tuberculosis

“Die Aetiologie der Tuberculose”
Robert Koch (1843-1910)
Berlin, March 24, 1882

Mycobacterium tuberculosis
Mycobacterium tuberculosis

Molecular typing → many subgroups

The most predominant: Beijing strains
Spoligotyping (spacer-oligo-typing)
Molecular epidemiology in Indonesia:

Many different genotypes

Beijing strains the most predominant (33%)
Patient studies –
Beijing strains compared to other strains:

Cohort study – 818 patients
• Similar disease presentation
• Beijing ~ twice as many treatment failures
• Also when corrected for drug resistance

Long-term follow-up – 200 patients
• Beijing - more recurrent TB
• More lung damage
Beijing strains in invitro-studies

• Biochemical properties:
  ↑virulence: α crystalyn
  ↑latency: TAG
• Immunogenicity:
  ↓ immune recognition
  ↑ pro inflammatory cytokine
• Animal model:
  ↑ virulence: bacillary load, histopathology
Beijing strains more drug resistant

- ethambutol
- FQ
- PZA
- PZase
- embCAB eiwitten
- embB
- gyrase
- FQ
- Rifampicin
- rpoB
- RNA polymerase α β β' σ
- mRNA
- activated INH isoNAD
- katalase
- Detoxification of organic peroxides
- alkyl hydroperoxidase
- Enoyl ACP
- celwallsynthesis
- Detoxification of organic peroxides

- 3.1 times
- 1.6 times
- 2.2 times
## Follow up results

<table>
<thead>
<tr>
<th></th>
<th>Beijing</th>
<th>non-Beijing</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(273 patients)</td>
<td>(545 patients)</td>
<td></td>
</tr>
<tr>
<td>After 2 months treatment</td>
<td></td>
<td></td>
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<tr>
<td>Sputum microscopy performed (no. patients)</td>
<td>243 (89.0%)</td>
<td>499 (91.6%)</td>
<td></td>
</tr>
<tr>
<td>AFB-positive</td>
<td>39 (14.3%)</td>
<td>72 (13.2%)</td>
<td>1.08 (0.75-1.55)</td>
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<tr>
<td>Sputum culture performed (no. patients)</td>
<td>172 (63.0%)</td>
<td>374 (68.6%)</td>
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<tr>
<td>Culture pos for <em>M. tuberculosis</em>, no. patts (%)</td>
<td>39 (14.3%)</td>
<td>68 (12.5%)</td>
<td>1.14 (0.79-1.65)</td>
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<tr>
<td>After 6 months treatment</td>
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<tr>
<td>Sputum microscopy performed (no. patients)</td>
<td>185 (67.8%)</td>
<td>374 (68.6%)</td>
<td></td>
</tr>
<tr>
<td>AFB-positive</td>
<td>11 (4.0%)</td>
<td>16 (2.9%)</td>
<td>1.37 (0.65-2.92)</td>
</tr>
<tr>
<td>Sputum culture performed (no. patients)</td>
<td>150 (54.9%)</td>
<td>300 (55.0%)</td>
<td></td>
</tr>
<tr>
<td>Culture pos for <em>M. tuberculosis</em>, no. pts (%)</td>
<td>36 (13.2%)</td>
<td>37 (6.8%)</td>
<td>1.94 (1.26-3.00)</td>
</tr>
</tbody>
</table>
“co-evolution”

Variation in one gene increased the risk of getting TB caused by Beijing strains:

Strong association between Beijing and NRAMP-polymorphisms

Variation in one gene increased the risk of getting TB caused by Beijing strains:

Strong association between Beijing and NRAMP-polymorphisms
Exposure to Beijing strain

- Transmission

Latent TB (infection)

- Disease progression

Active TB (disease)

- TB treatment

Treatment failure

- Reccurent TB
Acknowledgement

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Thank you

Dank U wel

Terimakasih