GeneXpert MTB/RIF in the Diagnosis of Pulmonary TB Among Severely Malnourished Hospitalized Malawian Children

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Background

TB dx in children challenging
- Paucibacillary/smear negative, issues w/ obtaining samples
- Clinical presentation often vague

Recent advances
- Xpert MTB/RIF in pediatric patients w/suspected TB
  - 75% sensitivity, 98-100% specificity compared to Cx

Limited data describing the accuracy of Xpert MTB/RIF in severely malnourished children


Study Procedure

Hospitalized children 6 - 60 months with severe malnutrition*

CXR (read by 2 blinded reviewers)

TB exposure (TST > 5 mm, TB contact)

TB signs/symptoms
- Fever, Cough, Lethargy/Dec Playfulness

HIV status

Induced sputum (2 per child)
- AFB smear/liquid culture
- Xpert MTB/RIF

Follow-up at 6 weeks

Assigned Case Definitions (Graham, et al. 2012)
- Confirmed, Probable, Possible, or Unlikely TB disease

*WHO guidelines: W/H < - 3 SD, MUAC < 115 mm, or Bilateral edema
## Results

### Characteristics of Study Participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N= 300</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in months, mean (SD)</td>
<td>20.7</td>
<td>(+/- 10.9)</td>
</tr>
<tr>
<td>Female</td>
<td>145</td>
<td>(51.3)</td>
</tr>
<tr>
<td>WFH Z , mean (SD)</td>
<td>-3.0</td>
<td>(+/- 1.2)</td>
</tr>
<tr>
<td>HIV Infected</td>
<td>47</td>
<td>(15.7)</td>
</tr>
<tr>
<td>TB Exposure</td>
<td>43</td>
<td>(14.3)</td>
</tr>
<tr>
<td>TST &gt;= 5 mm</td>
<td>40</td>
<td>(13.9)</td>
</tr>
<tr>
<td>CXR (certain TB)</td>
<td>48</td>
<td>(16.1)</td>
</tr>
<tr>
<td>TB tx initiated</td>
<td>132</td>
<td>(44.0)</td>
</tr>
<tr>
<td>Death</td>
<td>28</td>
<td>(9.3)</td>
</tr>
</tbody>
</table>

- **17 (36%) New Dx HIV**
- **Only 1 was offered IPT**
- **19% in HIV Infected**
Study Profile

Patients Enrolled
300

1 induced sputum
300

295 w/ 2 induced sputums

Confused TB
2 (.7%)
2 initiated treatment

Probable TB
20 (6.7%)
16 initiated treatment

Possible TB
197 (66%)
91 initiated treatment

Unlikely TB
81 (27%)
14 initiated treatment

Likely prevalence of TB 7.4%

1 smear pos
2 GeneXpert pos

0 smear pos
1 GeneXpert pos

Low microbiologic confirmation
Discussion

- Low microbiologic confirmation of TB
- Prevalence of TB likely closer to 7.4% (Confirmed + Probable TB)
- 25% HIV + prevalence in children with Probable TB
- Improved HIV screening and TB prevention services needed
  - 36% w/ HIV were new diagnoses
  - 98% w/ TB contacts were not offered IPT
- Need for better TB diagnostics in severely malnourished children
## Clinical Case Definitions

<table>
<thead>
<tr>
<th>Confirmed TB disease</th>
<th>Probable TB disease</th>
<th>Possible TB disease</th>
<th>Unlikely TB disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>• &gt; 1 sign/symptom suggestive of TB* disease AND</td>
<td>• &gt; 1 sign/symptom suggestive of TB disease AND</td>
<td>• &gt; 1 sign/symptom suggestive of TB disease AND</td>
<td>• Symptomatic but not fitting the other definitions and no alternative diagnosis established</td>
</tr>
<tr>
<td>• microbiological confirmation (MTB Culture)</td>
<td>• + CXR AND</td>
<td>• EITHER - CXR but + exposure or + TST or clinical response to anti-TB tx</td>
<td></td>
</tr>
<tr>
<td><em>Cough &gt; 2 weeks (not responding to abx)</em></td>
<td>• + exposure or +TST or clinical response to anti-TB tx</td>
<td>• OR + CXR, but no exposure and - TST</td>
<td></td>
</tr>
<tr>
<td>Fever &gt; 1 weeks</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lethargy/decreased playfulness</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Weight loss</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

TB Symptoms by Clinical Case Definitions

- Cough > 2 weeks not responding to antibiotics
  - Confirmed/Probable TB: 32%
  - Possible TB: 13%
  - Unlikely TB: 4%

- Fever > 1 week
  - Confirmed/Probable TB: 41%
  - Possible TB: 26%
  - Unlikely TB: 22%

- Lethargy/Reduced Playfulness
  - Confirmed/Probable TB: 86%
  - Possible TB: 90%
  - Unlikely TB: 90%