Global Epidemiology of TB in Children, Adolescents and Pregnant Patients

Lindsay H Cameron MD MPH
Assistant Professor
Pediatric Infectious Diseases
Baylor College of Medicine/Texas Children’s Hospital

Conflicts of Interest

• I have no conflicts of interest to disclose.
Outline

• Review Tuberculosis (TB) definitions
• Discuss limitations in estimating TB in children & pregnant patients
• Provide an overview of TB Epidemiology in children & pregnant patients
• Discuss the impact of the COVID-19 pandemic on TB
• Case Based Discussion
• Q&A

• TB disease is > 9,000 years old
• Has killed ~ 1 billion people in the past 200 years
Clinical Case

• 14 yo F, US born
• Was living with mother in Reynosa, Mexico
• Developed TB symptoms in April 2020
  • Shortness of breath
  • Exercise intolerance
  • 3 kg weight loss
  • Cough
• Started on RIPE therapy
• Culture confirmed pan-susceptible TB on 4/24/20, 4/25, and 4/26
• Moved to the US in May 2020  
  • Clinical symptoms improved  
• Negative cultures: 3 in May, 1 in June, 1 in July  
• Bi-national TB treatment program:  
  • video DOT during week, self-administered on weekends  
  • 13 missed doses  
• Serial CXRs (8/14 with some improvement, 12/7 with blebs)  

• Complicated social setting, diagnosed with depression  
• Moved to the U.S. to live with maternal grandmother
• Jan 2021, developed shortness of breath
• Taken to OSH
  • Concern for pneumothorax
  • → chest tube placed, then removed

• Transferred to TCH

---

**Evaluation**

• Exam
  • Weight 84 lbs (38.5kg); 0.7%
  • Thin, flat affect
  • decreased breath sounds diffusely in the right lung fields

• Labs:
  • Anemic (Hb 10.4), normal LFTs

• TSPOT:
  • 8/11 spots

• HIV negative

• Sputa collected x3
  • Smear negative
• Continued on RIPE therapy
  • Mycobacterial cultures negative
• Chest tube placed for acute onset SOB
• Nutritional rehabilitation
Surgical Intervention (Feb 2020)

- Right thoracotomy
- Blebectomy
- Pleurodesis

- Findings:
  - Moderate adhesions of the RUL, RML, RLL to the chest wall and diaphragm
  - Resection of the multiloculated RLL bleb
  - A mechanical pleurodesis
  - Excellent expansion of all lobes of R lung
  - Fibrin sealant over the staple lines & surface of the lung

Pleura Pathology & Microbiology

- Pleura, right lower lobe, blebectomy:
  - Markedly thickened pleura with adhesions, hemorrhage, granulation tissue formation and chronic (non-granulomatous) inflammation.

- Lung, right lower lobe, wedge biopsy:
  - Subpleural and pleural necrotizing and non-necrotizing granulomatous inflammation.
  - No acid fast organisms identified on Fite and AFB stains.

- Smear negative, cultures negative (6 weeks)
• Continued on
  • INH, RIF and ETH
  • No optic neuropathy
• X 4 additional months
• Discharged home (Hidalgo Co. HD)

• This case highlights the importance of prevention and treatment of TB Worldwide (& in children).
TB is a Disease of Poverty

• TB is often known as “a disease of the poor”

• “the burden of TB follows a strong socioeconomic gradient both between and within countries, and also within the poorest communities of countries with high TB incidence.”

• ~95% of TB cases worldwide occur in low-middle income countries

TB Strikes the Poor

These World Health Organization data show the pattern: Across the globe, poverty and tuberculosis go hand in hand. In wealthy countries, rapid detection prevents spread, and effective drugs cure most cases. But in poor and middle-income nations where crowded conditions foster disease and affordable treatment is hard to find, TB kills more than one million people every year.

TB Prevalence and Gross Domestic Product in the World’s 10 Most Populous Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases of TB per 100,000 People, 2020</th>
<th>GDP per Capita (current USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indonesia</td>
<td>100</td>
<td>$1,189</td>
</tr>
<tr>
<td>Pakistan</td>
<td>150</td>
<td>$2,370</td>
</tr>
<tr>
<td>Nigeria</td>
<td>125</td>
<td>$1,835</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>175</td>
<td>$10,435</td>
</tr>
<tr>
<td>India</td>
<td>200</td>
<td>$3,670</td>
</tr>
<tr>
<td>China</td>
<td>225</td>
<td>$1,866</td>
</tr>
<tr>
<td>Russia</td>
<td>250</td>
<td>$6,535</td>
</tr>
<tr>
<td>Brazil</td>
<td>275</td>
<td>$2,370</td>
</tr>
<tr>
<td>Mexico</td>
<td>300</td>
<td>$1,593</td>
</tr>
<tr>
<td>U.S.</td>
<td></td>
<td>$53,593</td>
</tr>
</tbody>
</table>

https://www.nature.com/articles/d41586-022-01348-0
The Sityaya family in Khayelitsha, South Africa, all had tuberculosis, except for the baby, who received preventive treatment. Credit: Jonathan Torgovnik

https://www.nature.com/articles/d41586-022-01348-0

• How do we identify children at risk for TB?
TB Definitions

TB exposure:

TB Definitions cont.

• TB infection (TBI):
TB Definitions cont.

• TB disease:

Most M.TB is transmitted to children by adults (or adolescents)
A child newly diagnosed with TB is a sentinel event indicating recent transmission in a community.
Children with TB infection = reservoir for disease

How do we identify children at risk for TB?

- Immigration based screening
- TB risk factor based screening
  - Exposure to TB contact
  - Birth or extended travel to high-prevalence TB setting
  - Regular exposure to high-risk adult/setting
Probability of Infection

• Intimacy & duration of contact
• Infectiousness of source case
• Virulence of bacterial strain
• Shared environment
HHC, smear + → 60-80% infected
HHC, smear - → 30-40% infected

HIGH RISK

- 60% children infected < 3 months*
  - *TST conversion
- >80% <2 years: HHC, or close caregiver
- 50-70% CXR abnormalities
  - 60-80% <2 years
LESS RISK

- *complicated by poverty

---

![Image](image-url)

---

Table 3. The calculated risk of developing primary tuberculosis (TB) infection, compared to the calculated risk of being notified with TB-related disease or death following primary TB infection, within specific age groups.

<table>
<thead>
<tr>
<th>Age group, years</th>
<th>Calculated risk to develop primary TB infection*</th>
<th>Calculated risk to be notified with TB-related disease, following primary TB infection</th>
<th>Calculated risk to be notified with TB-related death, following primary TB infection</th>
<th>Relative TB-related mortality*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>&lt;1</td>
<td>11.9</td>
<td>6</td>
<td>0.6</td>
</tr>
<tr>
<td>1-4</td>
<td>10</td>
<td>5.6</td>
<td>1</td>
<td>12.1</td>
</tr>
<tr>
<td>5-9</td>
<td>20</td>
<td>3.8</td>
<td>0.3</td>
<td>9.1</td>
</tr>
<tr>
<td>10-14</td>
<td>10</td>
<td>6.4</td>
<td>0.5</td>
<td>9.1</td>
</tr>
<tr>
<td>15-24</td>
<td>30</td>
<td>10 (males)</td>
<td>1.5 (males)</td>
<td>16.7 (males)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13 (females)</td>
<td>2.6 (females)</td>
<td>39.4 (females)</td>
</tr>
</tbody>
</table>

* Indicates the calculated percentage of children who develop primary infection (tuberculin conversion) within a specific age group.
† Indicates the number of children notified with TB, as a percentage of the total number expected to have developed primary TB infection, within a specific age group.
‡ Indicates the number of children notified with death due to TB, as a percentage of the total number expected to have developed primary TB infection within a specific age group.
§ Indicates the percentage of TB-related mortality compared to all-cause mortality within a specific age group.

Data on primary TB infection were collected from the British MRC tuberculin skin test survey for London (1949–1950). This was converted into the number of children expected to develop primary infection within a specific age group, using national census data for London (1951). Data on TB-related disease and death were collected from TB notifications and death certificates for London (1945–1949). Absolute notification numbers were converted into percentages, using the number expected to develop primary infection within a specific age group as denominator and accepting that all notifications result from recent primary infection. Relative TB-related mortality was calculated from death certificates for England and Wales (1950), comparing TB-related mortality with all-cause mortality.
Risk of Infection → Disease

• Infants – HIGHEST RISK
  • 30-40% develop TB meningitis
  • 10-20% miliary disease

• Children <5 years
  • 10-20% (highest risk <2 years)

• Children 5-10 years “GOLDEN PERIOD”

• Adolescents → 10-20%

• Other risk groups:
  • primary or secondary immunodeficiency, malnutrition, renal disease, diabetes

TB in Adolescents vs. Children

**Adolescents**
- Reactivation of infection
- Adult type disease
- Often infectious
- Smear/culture/PCR +

**Children**
- Paucibacillary
- Most non-infectious
- Smear/culture/PCR negative
- Intrathoracic adenopathy
- Diagnosed clinically
TB Epidemiology Worldwide

GLOBAL TUBERCULOSIS REPORT 2021
WHO Global Report

• Reports annual estimates of Global TB:
  • Incidence, prevalence & mortality
  • Regional & country levels
    • 22 countries [195], 10 in Africa [54]
  • Age & gender
  • *No specific statistics in pregnant patients*

TB Incidence/Prevalence Worldwide

• Disaggregation by age (2012)
  • Adolescents/adults, > 15 years
  • Children (0-14 years)
  • Inclusion of child cases is limited
Prior Challenges, New Goals

• Limited focus on non-infectious TB

• New focus on child/maternal health (2012)
  • Increased surveillance, identification and reporting
  • Focus on development of enhanced diagnostics

Enhancing Childhood TB Estimates

• Improved health infrastructure
  • Integration of child/maternal health services

• Funding for contact investigations
  • *all infants & children living with a TB case

• Promotion of case-based recording
  • Age-specific data
ALL OF THIS “PROGRESS” WAS MADE... then...

The COVID-19 pandemic has reversed years of progress made in the fight to end TB

In 2020
- TB DEATHS INCREASED FOR THE FIRST TIME IN OVER A DECADE
- FEWER PEOPLE WERE DIAGNOSED AND TREATED OR PROVIDED WITH TB PREVENTIVE TREATMENT
- FEWER RESOURCES FOR ESSENTIAL TB SERVICES AND TB R&D

Actions to mitigate and reverse the impact of the COVID-19 pandemic on access to essential TB services are urgently needed
COVID Pandemic, Impact on Global TB

• TB funding ↓ from 5.8 billion → 5.3 billion
  • (<50% of need)

• Monetary & HR shortages
  • Reduction in TB case detection & reporting

• Supply- and demand-side disruptions
  • Affected both diagnostic & treatment services
BCG Vaccination Worldwide

• Provided by 154 countries
  • 53 > 95%
  • 31 reported > 5% reduction in coverage (due to funding)
TB Incidence
18% Reduction in TB reporting

FIG. 1
Global trend in case notifications of people newly diagnosed with TB, 2016–2020

7.1 million (2019) → 5.8 million (2020)
• 9.9 million new cases *(2020)*
  • 30 HB countries → 86% of estimated incident cases
  • 127/100K
• Most new cases reported in:
  • SE Asia (43%)
  • Africa (25%)
  • Western Pacific (18%)

*Fig. 11*
Estimated TB incidence in 2020, for countries with at least 100 000 incident cases
The eight countries that rank first to eighth in terms of numbers of cases, and that accounted for two thirds of
global cases in 2020, are labelled.

India (26%), China (8.5%), Indonesia (8.4%),
Philippines (6.0%), Pakistan (5.8%),
Nigeria (4.6%), Bangladesh (3.6%), South Africa (3.3%)
Central African Republic, Democratic People’s Republic of Korea, Lesotho, the Philippines and South Africa
**Women 33%**

**Children 11%**

(1.1 million)

Highest burden of new TB cases – in adult males (56%)

---

**TB Incidence in Children**

- Mathematic model, estimate (2014)
  - ~1,000,000 (range: 900,000 – 1,100,000) TB cases
  - 10% of the cases
- ~32,000 with MDR-TB
- ~53 million TB infection cases
  - (in the 22 HB countries)
MDR/RR-TB Incidence Worldwide

- Incidence is stable
  - 3-4% new infections
  - 18-21% previously treated
- Highest proportion of cases (>50%)
  - Countries of the former Soviet Union

Global burden of drug-resistant tuberculosis in children: a mathematical modelling study

Peter J Dodd, Charalampos Skirmianis, James A Seddon

WHO Global Project DR Surveillance 1988-2014
• 2014
  • 6.9% INH R
  • 2.9% MDR
  • 4.7% XDR
- Estimated incidence
- 847K R cases
  - 25K MDR
• ~67 million children infected
  • 2 million MDR
  • 101,000 XDR
• Many children undiagnosed
  • At risk of developing DR disease
    • In childhood
    • In adulthood
Tuberculosis Epidemiology in Children in the U.S.
Epidemiology of tuberculosis among children and adolescents in the USA, 2007–17: an analysis of national surveillance data

Tori I. Cowger, Jonathan M Wortham, Deron C Burton

Lancet Public Health 2015; 4:e506-16
### Reported in US states

<table>
<thead>
<tr>
<th>Age, years</th>
<th>US born (n=3520)</th>
<th>Non-US born (n=1655)</th>
<th>Total (n=5175)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>2377 (85%)</td>
<td>919 (56%)</td>
<td>3296 (75%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;1</td>
<td>448 (12%)</td>
<td>26 (2%)</td>
<td>474 (9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1-4</td>
<td>1503 (43%)</td>
<td>253 (15%)</td>
<td>1756 (34%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5-14</td>
<td>1026 (29%)</td>
<td>640 (32%)</td>
<td>1666 (32%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>15-17</td>
<td>543 (15%)</td>
<td>736 (45%)</td>
<td>1279 (25%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Reported in US-affiliated islands

<table>
<thead>
<tr>
<th>Age, years</th>
<th>US born (n=397)</th>
<th>Non-US born (n=897)</th>
<th>Total = 1294</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>2377 (85%)</td>
<td>919 (56%)</td>
<td>3296 (75%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;1</td>
<td>448 (12%)</td>
<td>26 (2%)</td>
<td>474 (9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1-4</td>
<td>1503 (43%)</td>
<td>253 (15%)</td>
<td>1756 (34%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5-14</td>
<td>1026 (29%)</td>
<td>640 (32%)</td>
<td>1666 (32%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>15-17</td>
<td>543 (15%)</td>
<td>736 (45%)</td>
<td>1279 (25%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Total reported to the NTSS

<table>
<thead>
<tr>
<th>Age, years</th>
<th>US born (n=3520)</th>
<th>Non-US born (n=1655)</th>
<th>Total (n=5175)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>2377 (85%)</td>
<td>919 (56%)</td>
<td>3296 (75%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;1</td>
<td>448 (12%)</td>
<td>26 (2%)</td>
<td>474 (9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1-4</td>
<td>1503 (43%)</td>
<td>253 (15%)</td>
<td>1756 (34%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5-14</td>
<td>1026 (29%)</td>
<td>640 (32%)</td>
<td>1666 (32%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>15-17</td>
<td>543 (15%)</td>
<td>736 (45%)</td>
<td>1279 (25%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

### Race or ethnicity

<table>
<thead>
<tr>
<th>Race or ethnicity</th>
<th>US born (n=3520)</th>
<th>Non-US born (n=1655)</th>
<th>Total (n=5175)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian</td>
<td>468 (13%)</td>
<td>581 (30%)</td>
<td>1059 (20%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Black</td>
<td>861 (25%)</td>
<td>489 (30%)</td>
<td>1350 (26%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1659 (47%)</td>
<td>444 (27%)</td>
<td>2103 (41%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Native American or</td>
<td>107 (3%)</td>
<td>107 (2%)</td>
<td>214 (2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Alaska Native</td>
<td>100 (3%)</td>
<td>47 (3%)</td>
<td>147 (3%)</td>
<td>0.9896</td>
</tr>
<tr>
<td>Native Hawaiian or</td>
<td>107 (2%)</td>
<td>2 (1%)</td>
<td>109 (2%)</td>
<td>0.0849</td>
</tr>
<tr>
<td>other Pacific Islander</td>
<td>100 (3%)</td>
<td>47 (3%)</td>
<td>147 (3%)</td>
<td>0.9896</td>
</tr>
<tr>
<td>Two or more races</td>
<td>36 (1%)</td>
<td>9 (1%)</td>
<td>45 (1%)</td>
<td>0.0849</td>
</tr>
<tr>
<td>White</td>
<td>277 (8%)</td>
<td>65 (4%)</td>
<td>342 (7%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
### Nativity of parents or primary guardians

<table>
<thead>
<tr>
<th>Nativity of Parents or Primary Guardians</th>
<th>US Born (n=3520)</th>
<th>Non-US Born (n=1655)</th>
<th>Total (n=5175)</th>
<th>P value $^5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both US born</td>
<td>604 (20%)</td>
<td>40 (4%)</td>
<td>644 (17%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Both non-US born</td>
<td>1205 (41%)</td>
<td>526 (57%)</td>
<td>1731 (44%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non-US born and US born</td>
<td>284 (10%)</td>
<td>19 (2%)</td>
<td>303 (8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>US born and unknown</td>
<td>280 (9%)</td>
<td>15 (2%)</td>
<td>295 (8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Non-US born and unknown</td>
<td>355 (12%)</td>
<td>224 (24%)</td>
<td>579 (15%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Both unknown</td>
<td>249 (8%)</td>
<td>95 (10%)</td>
<td>344 (9%)</td>
<td>0.0654</td>
</tr>
</tbody>
</table>

### Primary reason evaluated for tuberculosis

<table>
<thead>
<tr>
<th>Primary reason evaluated for tuberculosis</th>
<th>US Born (n=3520)</th>
<th>Non-US Born (n=1655)</th>
<th>Total (n=5175)</th>
<th>P value $^5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis symptoms</td>
<td>1220 (35%)</td>
<td>698 (42%)</td>
<td>1918 (37%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Contact investigation</td>
<td>1456 (41%)</td>
<td>159 (10%)</td>
<td>1615 (31%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Abnormal chest x-ray</td>
<td>550 (16%)</td>
<td>360 (22%)</td>
<td>910 (18%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Immigration medical exam</td>
<td>208 (13%)</td>
<td>208 (4%)</td>
<td>416 (8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Incidental laboratory result</td>
<td>152 (4%)</td>
<td>72 (4%)</td>
<td>224 (4%)</td>
<td>0.9576</td>
</tr>
<tr>
<td>Targeted testing</td>
<td>95 (3%)</td>
<td>104 (6%)</td>
<td>199 (4%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other†</td>
<td>16 (1%)</td>
<td>22 (1%)</td>
<td>38 (1%)</td>
<td>0.0006</td>
</tr>
</tbody>
</table>
• 68% pulmonary TB
  • 22% extra-pulmonary
• 39%, culture confirmed
  • 8% mono INH R
  • 1% RIF R
  • 1% MDR
• 80%, abnormal CXR
• <1% HIV+
• 91% completed treatment
• <1% mortality (n = 32)

Incidence

• Overall incidence, 1.0/100,000 person years
• Highest in < 1yr olds (1.9)
• Followed by adolescents (1.4)
• Age-specific incidence (10X) non-US born (9.0)
• Highest in Native Hawaiian/Pacific Islander (114.0)
  • High rates in Marshall Islands & Federated States of Micronesia
TB Mortality Worldwide
1st time >10 years, TB deaths have increased

Includes data from 197 countries & territories
TB 2nd → leading infectious cause of death
• 1.3 million TB deaths (HIV-) \textbf{(2020)}
  • 1.2 million \textbf{(2019)}
• 214K (HIV +) \textbf{(2020)}
  • 209K \textbf{(2019)}
• TB deaths ↑ in most 30 HB countries

• 85% of TB associated deaths: African and SE Asia
  • India: 38% of global TB deaths (HIV negative)
• Among the HIV negative (1.3 million)
  • 32% women
  • \textbf{16% children (<15 years)}
• HIV positive (214K)
  • 40% women
  • \textbf{9.8% children}
TB Mortality in Children

• Mathematic model, estimate (2014)

• Total deaths: 136,000 (range: 115,000-157,000)
  • 81,000 (range: 69,000-93,000) (HIV negative children)
  • 7% of total deaths
  • 55,000 (range: 50,000-60,000) (HIV positive children)

• Case fatality rate: 13.6%

Tuberculosis Epidemiology in Pregnancy
Risk of TB during Pregnancy

• Increased maternal mortality
• 2x increase in:
  • premature birth
  • LBW infant
  • IUGR
• 6x risk
  • Perinatal death (*especially in HIV-co-infection)
• Risk of transmission to infant
  • Early post-partum, vulnerable time → 2x risk of TB
  • South African study:
    • Pregnant patients, active TB
    • 15% of infants infected w/in 3 weeks
• True burden of TB in pregnant patients worldwide is unknown

Tuberculosis in pregnancy: an estimate of the global burden of disease

Jordan Sugarman, Charlotte Colvin, Allisyn C. Moran, Olivia Oxlade
• 216,500 pregnant patients with TB *(2011)*
Table 2: Total number of active tuberculosis cases in pregnant women, rate per 1000 pregnant women and percentage of global burden by WHO region and combined

<table>
<thead>
<tr>
<th>Region</th>
<th>Mean (95% uncertainty range)</th>
<th>Rate per 1000 pregnant women (95% uncertainty range)</th>
<th>Percentage of global burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>All countries combined</td>
<td>215,500 (192,100-247,000)</td>
<td>2.1 (1.8-2.4)</td>
<td></td>
</tr>
<tr>
<td>African Region</td>
<td>89,400 (74,200-110,500)</td>
<td>3.6 (3.0-4.5)</td>
<td>41%</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>48,000 (39,000-60,000)</td>
<td>0.4 (0.3-0.5)</td>
<td>2%</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>28,500 (19,700-41,900)</td>
<td>2.3 (1.6-3.4)</td>
<td>13%</td>
</tr>
<tr>
<td>European Region</td>
<td>49,000 (38,000-63,000)</td>
<td>0.6 (0.5-0.8)</td>
<td>2%</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>67,500 (52,000-87,100)</td>
<td>2.4 (1.9-3.1)</td>
<td>21%</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>21,400 (19,400-23,700)</td>
<td>1.1 (1.0-1.2)</td>
<td>10%</td>
</tr>
</tbody>
</table>

Table 3: Total number of active tuberculosis cases in pregnant women, rate per 1000 pregnant women and percentage of global burden among pregnant women in the 22 high tuberculosis burden countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Mean (95% uncertainty range)</th>
<th>Rate per 1000 pregnant women (95% uncertainty range)</th>
<th>Percentage of global burden*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afghanistan</td>
<td>6100 (5200-11,000)</td>
<td>7.2 (3.5-12.8)</td>
<td>2.8%</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>5000 (4300-5800)</td>
<td>3.5 (1.8-4.4)</td>
<td>3.3%</td>
</tr>
<tr>
<td>Brazil</td>
<td>800 (400-1600)</td>
<td>0.4 (0.3-0.7)</td>
<td>0.6%</td>
</tr>
<tr>
<td>Cambodia</td>
<td>1700 (1600-1900)</td>
<td>5.5 (4.0-7.0)</td>
<td>1.0%</td>
</tr>
<tr>
<td>China</td>
<td>9000 (8200-11,000)</td>
<td>0.7 (0.6-0.8)</td>
<td>2.4%</td>
</tr>
<tr>
<td>DR Congo</td>
<td>16,200 (8700-29,000)</td>
<td>7.2 (4.9-12.5)</td>
<td>7.5%</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>3600 (2050-6500)</td>
<td>3.7 (1.9-5.6)</td>
<td>3.7%</td>
</tr>
<tr>
<td>India</td>
<td>66,000 (50,000-82,000)</td>
<td>2.7 (2.3-3.1)</td>
<td>29%</td>
</tr>
<tr>
<td>Indonesia</td>
<td>9500 (4700-14,000)</td>
<td>3.9 (3.4-4.6)</td>
<td>4.4%</td>
</tr>
<tr>
<td>Kenya</td>
<td>2800 (2200-3700)</td>
<td>3.8 (2.3-6.4)</td>
<td>2.0%</td>
</tr>
<tr>
<td>Mozambique</td>
<td>4500 (2080-4700)</td>
<td>5.8 (2.1-10.4)</td>
<td>2.9%</td>
</tr>
<tr>
<td>Myanmar</td>
<td>2050 (1300-2800)</td>
<td>3.9 (3.3-5.8)</td>
<td>1.2%</td>
</tr>
<tr>
<td>Nigeria</td>
<td>10,900 (9000-11,700)</td>
<td>3.1 (2.6-4.6)</td>
<td>5.0%</td>
</tr>
<tr>
<td>Pakistan</td>
<td>16,000 (7,200-18,800)</td>
<td>6.1 (5.5-7.2)</td>
<td>1.3%</td>
</tr>
<tr>
<td>Philippines</td>
<td>6600 (5700-7500)</td>
<td>2.7 (2.4-3.2)</td>
<td>1.0%</td>
</tr>
<tr>
<td>Russia</td>
<td>1200 (1000-1400)</td>
<td>0.9 (0.4-1.8)</td>
<td>0.5%</td>
</tr>
<tr>
<td>South Africa</td>
<td>8600 (6900-10,000)</td>
<td>10.3 (8.5-12.2)</td>
<td>13%</td>
</tr>
<tr>
<td>Tanzania</td>
<td>10,000 (8200-10,700)</td>
<td>5.2 (4.3-6.3)</td>
<td>1.4%</td>
</tr>
<tr>
<td>Thailand</td>
<td>5200 (400-9300)</td>
<td>0.9 (0.4-3.6)</td>
<td>0.2%</td>
</tr>
<tr>
<td>Uganda</td>
<td>2650 (1800-4300)</td>
<td>2.1 (1.3-3.8)</td>
<td>1.2%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>960 (700-1200)</td>
<td>0.8 (0.5-1.5)</td>
<td>0.4%</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>1600 (1000-1800)</td>
<td>7.5 (4.9-11.0)</td>
<td>1.1%</td>
</tr>
<tr>
<td>Total</td>
<td>196,300 (149,000-264,000)</td>
<td>3.5 (3.2-3.7)</td>
<td>77%</td>
</tr>
</tbody>
</table>

*Total percentage does not sum to 100% because it only shows % of global burden in pregnant women for each of the 22 high tuberculosis burden countries.
Improvements → TB Elimination

• Redirect resources towards TB prevention & treatment

• Enhanced TB screening at household level
  • Especially among children < 5 years
  • Enhance contact tracing

• Continue BCG vaccination of infants

Improvements → TB Elimination

• Increase treatment of those with TB infection –
  • discussed in a future webinar

• Increased access to shorter (1–3 months) regimens (TB infection)
  • discussed in a future webinar
Clinical Case Discussion
Clinical Case – Family Cohort (7+)

- Refugees from Afghanistan
  - Urgently evacuated
- Arrived to US in early 2022
  - Father
  - Mother (pregnant at time of arrival)
  - 5 children (2 yo, 3yo, 5 yo, 8 yo, 9yo)

- Overseas pre-immigration screening not available
- Family tested for TB upon arrival to the U.S.

TB in Afghanistan?
Thousands of Afghans were forced to leave their homes this year as fighting intensified.

Number of people displaced due to conflict, by month

Source: UNOCHA
TB in Afghanistan

• A major health problem
• Lack of recent statistics
  • 2016: 65K cases, 11K deaths
  • 2020: 73K cases
    • 15,000 children
    • 11,000 TB related deaths
• 2021 – estimated 600K cases!
AFGHANISTAN
14 million people going hungry

One-third of Afghanistan’s population are facing food insecurity, including two million children who are already malnourished, according to the WFP.

14 million (34%) Afghans are food insecure
2 million children are malnourished

Food insecurity level
Minimal
Stressed
Crisis
Emergency
Famine

Source: World Food Programme (WFP), Food Security & Nutrition Analysis Unit, updated August 26, 2022

Correspondence
Highlighting the forgotten: Tuberculosis amidst the humanitarian crisis and COVID-19 in Afghanistan

TB CASES (including DR)
? Parents

- Dad – (asymptomatic)
  - Normal CXR, +IGRA, receiving 3HP

- Mom – (asymptomatic)
  - +IGRA (at end of pregnancy)
  - CXR with RUL calcification, otherwise normal

Case Discussion

- Management of the mother (during pregnancy)?
- Following delivery (now breastfeeding)?
• Mom – (asymptomatic)
  • +IGRA *(at end of pregnancy)*
  • CXR with RUL calcification, otherwise normal
  • Sputa collected: smear negative, NAAT negative, cultures negative to date (4 weeks)

Mother

• *Treat or not treat? For infection or disease?*
Children

• 2mo, 2 yo, 3yo, 5 yo, 8 yo, 9yo

• Should they all be tested for TB infection? If so, how?

Children – upon arrival to U.S.

• 2mo, 2 yo, 3yo, 5 yo, 8 yo, 9yo

• 2mo
  • asymptomatic, no test of infection to date

• 2yo, 3yo, 5 yo, 8 yo, 9yo
  • all asymptomatic, +IGRAs
• All referred to the TCH TB Clinic

Children

• 2mo
  • asymptomatic, no test of infection, normal exam & CXR
  • Recommended timing of a test of infection?
  • Recommended treatment?

• 2yo
  • asymptomatic, +IGRA, normal exam & CXR
  • Recommended treatment for infection?

• 3yo, 5 yo, 8 yo
  • all asymptomatic, +IGRAs, normal exams & CXRs
  • Recommended treatment for infection?
Children

• 2mo
  • asymptomatic, no test of infection, normal exam & CXR
  • PPD to be placed @ 3 mo of age
  • receiving INH biweekly

• 2yo
  • asymptomatic, +IGRA, normal exam & CXR
  • Receiving daily RIF

• 3yo, 5 yo, 8 yo
  • all asymptomatic, +IGRAs, normal exams & CXRs
  • Receiving 3HP

TB Clinic Evaluation

• Interviewed with a Pashto interpreter

• No known contacts with TB

• “has felt warm at night, + night sweats”

• “no cough, no change in activity”
Physical Exam

• Afebrile, Weight 25kg (7%) ↓ 1 kg

• Small for age, thin

• No BCG scar

• Normal pulmonary exam
• How should he be managed?

Management

• HIV negative

• Cultures & NAAT obtained in field
  • Negative smear, +NAAT

• Started on RIPE therapy
F/U 2 months

- Resolved fever/night sweats
- Weight +2 kg
- Pansusceptible isolate
  - PZA & EMB discontinued

• Final thoughts/discussion from panelists.
**Clinical Case**

- 6yo M, Guatemalan immigrant, BCG immunized
  - Arrived to Houston in July, TX 2021
  - Father came to work for a construction company
    - (3 year term)
  - Mother and 2 siblings remain in rural Guatemala
  - Father speaks Kiche’ (some Spanish)
  - Child only speaks Kiche’

- Developed a soft tissue swelling in R paraspinal region (December 2021)
  - No fevers/systemic symptoms
- Seen by PCP
  - Positive quantiferon (0.87, 0.75)
• Referred to Dermatology & TB Clinic

TB in Guatemala?

• Incidence/prevalence in:
  • rural vs. urban areas?
- 25 cases/100,000 (WHO)
- 4,900 cases in 2020
  - 530 children
  - 410 TB associated deaths
- Likely underestimated
  - Rural>>>urban areas

**CASE REPORT**

**Delays in diagnosis and treatment of extrapulmonary tuberculosis in Guatemala**

Pooja Ajay Shah, 1 Merida Coj, 2 Peter Rohloff 3, 5

**Patient’s perspective**

This all started when I was working as a storekeeper. I began to feel some strange symptoms, like the fever and the growths that appeared around my neck. I was worried, but I didn’t know what to do. I didn’t have a solution. I went to many doctors, and they asked for tests but I could not afford them. I am so thankful that when I came to this clinic, you fought for me. The doctors and the compañera (patient care navigator) did a great favor for me by getting me to the hospital in the capital. Then, in the hospital they did all the tests I needed and finally figured out what was happening. They told me I had tuberculosis. The truth is, when I went to the hospital, I was hopeless. But I thank God that it worked out. Now I am very satisfied with the treatment I received.
Learning points

- In a country with a medium incidence of tuberculosis (TB; 25 cases per 100,000 people), health system segmentation can lead to significant delays in diagnosis and treatment of a classic clinical presentation of extrapulmonary TB.
- Vertical healthcare programmes, in contrast to integrated care, can be highly inefficient, due to provision of redundant testing and incomplete preventative care.
- Public–private partnerships can be employed to overcome some of the inefficiencies in a highly segmented health system, including shortcomings in the laboratory referral network.
- Indigenous people in Guatemala experience poor healthcare access and health outcomes due to barriers of poverty, language and rural residence.
- Patient accompaniment provides a potential solution to the barriers of health system segmentation faced by marginalised populations.

Clinical case Cont.

- Afebrile, normal RR
- <3% weight & height
- Poor dentition
- + murmur
- Decreased BS on R
- No HSM
- Non tender back swelling
• *How should he be managed?*
Radiologic Diagnosis: Empyema necessitans

• +/- contiguous osteomyelitis of the R 10th rib
• L axillary adenopathy
• R hilar and mediastinal adenopathy
• Multifocal tree-in-bud opacities and nodules
  • Throughout R lung

• Next steps in management?
IR Drainage

• 80mL, pink tinged purulent fluid drained
• 4 pleural biopsies obtained

Diagnostics

• HIV negative
• Repeat QFT: 1.9, 1.76
• Pleural fluid
  • Smear negative (degenerated/necrotic debris on pathology)
  • MTB PCR positive
  • Cultures pending

• Father’s chest radiograph (TCH) → NORMAL
• How should the patient be managed?

Management

• Started on RIPE therapy
• + prednisone x4 weeks → taper
Mycobacterial Culture Results

• *Mycobacterium tuberculosis* isolated on culture (19 days)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration</th>
<th>Susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>0.1 ug/mL</td>
<td>Suscept</td>
</tr>
<tr>
<td>Rifampin</td>
<td>1.0 ug/mL</td>
<td>Suscept</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>5.0 ug/mL</td>
<td>Suscept</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>100 ug/mL</td>
<td>Suscept</td>
</tr>
</tbody>
</table>

Follow-up – 1 month
Follow-up – 2 months
• Final thoughts/discussion from panelists.

Clinical Case

• 2 mo, U.S. born, ex-full term M
• Asymptomatic

• Exposed to father
  • Household contact
  • Symptomatic x2 months
  • Smear positive
  • Xpert MTB PCR positive
• Moved to the U.S. from Cameroon in early 2021
• *Eek! Based on this what is the infant’s risk?*

**Evaluation**

• Well appearing
• Normal exam
• *Quantiferon >10, >10*

• *Does a “wicked positive” QFT suggest disease over infection?*
• Hyper-aerated lungs are clear.
• No lymphadenopathy identified.

Is the lung hyper-aeration concerning?

Admitted to TCH

• First morning gastric aspirates x3 collected
  • Smear negative
  • MTB PCR negative
  • Cultures pending
9 mm solid pulmonary nodule in LUL.

6 mm solid pulmonary nodule in LLL.
CNS Evaluation

• LP/CSF evaluation
  • WBC 16 (slightly elevated, L 72%)
  • RBC 2,000
  • Protein 99 (slightly elevated)
  • Glucose normal

• MRI brain w/o contrast
  • No evidence of TB meningitis

• Why is his treatment complicated?
Management

- PO Levofloxacin, 10 mg/kg, BID (4/27/22 - present)
- PO Isoniazid 150mg once daily (4/29/22 - present)
- PO Linezolid 90 mg daily (4/29/22 - present)
- IV Imipenem 100 mg q12 (4/29/22 - present)
- Augmentin (amoxicillin-clavulanate ES 40mg/kg dose) (4/29/22 - present)

Update: Source Case – Susceptibility

- Silent RIF mutation (molecular)
- DST – pan-susceptible
- Receiving RIPE therapy (Galveston Co HD)
Definitive Management

• RIPE therapy
• High dose RIF

• Final thoughts/discussion from panelists.
Question & Answer

References