Arresting Vertical Transmission of Hepatitis B (AVERT-HBV) in the DRC

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December 13th, 2021
Disclosures

• I have funding from the NIH, ASTMH/Burroughs-Wellcome Fund, Merck and Novavax (Phase III COVID vaccine trial in children)

• I receive research support from Gilead Sciences and Abbott Laboratories
Outline

• Background on the DRC
• HBV in the DRC
• The AVERT-HBV Study
## DRC vs. USA Statistics

**Statistics (2019)**

<table>
<thead>
<tr>
<th></th>
<th>DRC</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>89 million</td>
<td>328 million</td>
</tr>
<tr>
<td>Per capita income</td>
<td>$580</td>
<td>$65,279</td>
</tr>
<tr>
<td>Life expectancy (women/men)</td>
<td>62/59</td>
<td>81/76</td>
</tr>
<tr>
<td>Fertility rate</td>
<td>5.8 births per woman</td>
<td>1.7 births per woman</td>
</tr>
<tr>
<td>Infant mortality rate</td>
<td>66/1000 live births</td>
<td>5.6/1000 live births</td>
</tr>
<tr>
<td>Under 5 mortality rate</td>
<td>85/1000 live births</td>
<td>6.5/1000 live births</td>
</tr>
</tbody>
</table>

UNICEF 2019; World Bank 2019; CDC Health, U.S.
Outline

• Background on the DRC
• HBV in the DRC
• The AVERT-HBV Study
IDEEL lab – Malaria and HepC in the DRC

Dr. Jonathan Parr

Parr JB et al. JID 2017; Parr JB et al. CID 2018
Seroepidemiology of HBV in the DRC

• Study Design:
  • Cross-sectional survey
  • Dried blood spots (DBS) and survey information collected during the 2013-2014 DRC Demographic and Health Survey
    • >18,000 DBS stored at UNC in Dr. Meshnick’s lab
  • Randomly sampled 1,000 DBS from various provinces for HBsAg testing

• Study Procedures:
  • Determination/mapping of seroprevalence using HBsAg assay
  • Phylogenetic analyses
  • Risk factor analysis
  • Assessment of research use of Abbott ARCHITECT HBsAg Qualitative assay on DBS

Thompson P, Parr JB, et al. AJTMH 2019
Study Population

980 DBS samples tested for HBsAg from all provinces

- 703 adult DBS samples tested
  - 30 HBsAg+ adults
    - 2 adults with successful HBV genotyping
- 277 child DBS samples tested
  - 9 HBsAg+ children
    - 8 children with successful HBV genotyping

Thompson P, Parr JB, et al. AJTMH 2019
Hepatitis B in the Democratic Republic of the Congo

DRC overall prevalence: **3.3% (1.8-4.7%)**
- Adults: 3.7% (1.9-5.5)
- Children: 2.2% (0.3-4.1)

Comparison to U.S. Prevalence (2013): 0.3%

Province-level, weighted HBV prevalence, measured by HBsAg positivity

Vaccination and wealth were protective factors against HBV acquisition in children

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Crude OR (95% CI)</th>
<th>Wald p-value</th>
<th>Adjusted OR (95% CI)</th>
<th>Wald p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination of any kind</td>
<td>0.04 (0.005-0.40)</td>
<td>0.006</td>
<td>0.04 (0.00-1.03)</td>
<td>0.05</td>
</tr>
<tr>
<td>Wealth index score</td>
<td>0.45 (0.28-0.74)</td>
<td>0.002</td>
<td>0.85 (0.40-1.82)</td>
<td>0.67</td>
</tr>
</tbody>
</table>
HBV Prevention

Prevention of vertical transmission:
• HepB vaccine + HBIG at birth (90-95% effective)
• Antivirals for women with high-risk HBV (High viral load and/or HBeAg positivity)

Prevention of horizontal transmission:
• 3-dose vaccine series (>95% effective)
Barriers to Preventing Vertical Transmission of HBV in Africa

• Pregnant women aren’t routinely tested for HBV
• Antivirals are available through HIV programs (active against both HIV and HBV)...but only given to HIV+ women
• Birth dose vaccine is not given to infants
  • Only 10% of African children receive a birth dose
• HBIG is not available
  • Not recommended by the WHO
Outline

• Background on the DRC
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Preventing Vertical Transmission: The AVERT-HBV Study

• Arresting Vertical Transmission of HBV in the DRC

• Goal: To prevent vertical transmission of HBV through:
  1) Identification and treatment of pregnant women with high-risk HBV
  2) Implementation of a birth dose vaccine for all exposed infants

• Novelty:
  • Builds upon the HIV framework to screen and treat pregnant women and their infants for HBV
  • Use of existing resources: study staff, laboratory equipment/personnel, HBV vaccine, antivirals

• Funding: Gillings Innovation Laboratory award (UNC School of Public Health)
AVERT Study Objectives

- **Primary objective**: To demonstrate the feasibility of adding hepatitis B testing and prevention measures to the existing HIV prevention platform in maternity centers in the DRC

- **Secondary objectives**:
  - Determine the incidence of vertical transmission of hepatitis B
  - Evaluate adherence to tenofovir therapy
  - Evaluate the timeliness of birth dose vaccination
AVERT Study Design/Setting

• Study design
  • Pilot feasibility study
  • Prospective cohort of 100 HBV-infected pregnant women and their infants (mother-infant dyads)

• Study setting
  • 2 maternity health centers in Kinshasa that together see >1,000 deliveries per month
AVERT Study Participants

• Pregnant women
  • Hepatitis B infected (HBsAg+)
  • <24 weeks’ gestation
  • Plan to receive care at one of the 2 maternity centers

• Hepatitis B-exposed infants
AVERT Study Procedures

1. Screening and enrollment
   • Screening for hepatitis B with HBsAg
   • Informed consent and enrollment

2. Determination of risk status
   • HBeAg and HBV DNA testing

3. Antivirals for high-risk women
   • 28-32 weeks’ gestation

4. Birth dose vaccine for all infants
   • Within 24 hours of life
AVERT Follow Up Visits

• Mothers
  • Low-risk: 24 weeks’ postpartum
  • High-risk: Monthly during pregnancy; 10 & 24 weeks’ postpartum

• Infants
  • 24 weeks: HBsAg and anti-HBs testing

Jolie Matondo, study nurse
Patrick Ngimbi, study physician
Sarah Ntambua, study nurse
Arresting vertical transmission of hepatitis B virus (AVERT-HBV) in pregnant women and their neonates in the Democratic Republic of the Congo: a feasibility study

Peyton Thompson, Camille E Morgan*, Patrick Ngimbi*, Kashamuka Mwandagaliwa, Noro L R Ravelomanana, Martine Tabala, Malongo Fathy, Bienvenu Kawende, Jérémie Muwonga, Pacifique Misingi, Charles Mbendi, Christophe Luhata, Ravi Jhaveri, Gavin Cloherty, Didine Kabo, Marcel Yotebieng, Jonathan B Parr

Summary

Background Hepatitis B virus (HBV) remains endemic throughout sub-Saharan Africa despite the widespread availability of effective childhood vaccines. In the Democratic Republic of the Congo, HBV treatment and birth-dose vaccination programmes are not established. We, therefore, aimed to evaluate the feasibility and acceptability of adding HBV testing and treatment of pregnant women as well as the birth-dose vaccination of HBV-exposed infants to the HIV prevention of mother-to-child transmission programme infrastructure in the Democratic Republic of the Congo.
AVERT-HBV Results: Hepatitis B screening

Overall HBV prevalence: 2.7% (2.2 - 3.2%)

4016 pregnant women assessed for eligibility

- 3907 screened negative for HBsAg

109 screened positive for HBsAg

- 18 excluded
  - 16 had a gestation of >24 weeks
  - 2 lost to follow-up

91 enrolled into study

- 37 did not complete study
  - 21 lost to follow-up
  - 16 withdrew from study
    - 11 voluntarily withdrew
    - 1 withdrawn by staff
    - 2 miscarriages
    - 1 stillbirth
    - 1 infant death

54 completed study

90 included in the study analysis

HBV screening of pregnant women and infant birth dose is feasible and acceptable

All 7 high-risk respondents reported tenofovir prophylaxis was “very acceptable”
Participant satisfaction

• 100% reported no problem for:
  • Ability to discuss own health concerns
  • Availability of medicines
  • Cost of services
  • Explanations of problems
  • Facility cleanliness
  • Privacy from others hearing your exam
  • Privacy from others seeing your exam
  • Treatment from staff

• Wait time: 2 of 54 reported as a minor problem
AVERT-HBV Care Continuum: Mothers

AVERT-HBV Care Continuum: Infants

68% of all infants followed to delivery received birth dose

77% of these were timely

Of all infants followed to delivery, 52% received timely birth dose

AVERT-HBV Conclusions

• It is feasible to add hepatitis B testing and prevention measures to the existing HIV infrastructure in the DRC.
• Using this two-pronged prevention approach, we prevented vertical transmission in all babies followed through 6 months!
• The overall prevalence of hepatitis B among pregnant women was 2.7%.
  • 11.1% of women with high-risk disease
• Challenges exist in implementing a timely birth dose vaccine and ensuring adherence to follow-up visits.
Delegation to promote universal birth-dose vaccination

Kinshasa, January 2020
Future directions/initiatives

• Disseminate findings from unpublished studies
• Publish results of HBV knowledge surveys
• Educational initiative
• Implementation of birth-dose vaccine study
• Future clinical trials related to prevention of vertical and horizontal transmission
Acknowledgements

UNC IDEEL Lab
Dr. Jon Juliano
Dr. Jonathan Parr
Dr. Sylvia Becker-Dreps
Alix Boisson
Camille Morgan
Sahal Thahir
Samantha Tulenko

UNC Pediatric Infectious Diseases
Dr. Toni Darville  Dr. Marsha Russell
Dr. Tom Belhorn  Dr. Matt Vogt
Dr. Zach Willis

Albert Einstein University
Dr. Marcel Yotebieng

Lurie Children’s Infectious Diseases
Dr. Ravi Jhaveri

Abbott Laboratories
Dr. Gavin Cloherty
Dr. Mary Kuhn
Vera Holzmayer

Kinshasa School of
Public Health
Prof Antoinette Tshefu
Prof Didine Kaba
Kashamuka Mwandagalirwa
Noro Ravelomanana
Bienvenu Kawende
Patrick Ngimbi  Sarah Ntambua
Martine Tabala  Jolie Matondo

University of Kinshasa
Dr. Charles Mbendi

UPC (Université Protestante du Congo)
Prof Samuel Mampunza
Linda James

DRC National AIDS  Control Program (PNLS)
Jérémy Muwonga
Franck Fwamba
Placide Welo

PEV
Dr. Elisabeth Mukamba
Christophe Luhata

Thanks to my funders!
ASTMH/Burroughs-Wellcome Fund
Gilead Sciences, Inc.
Merck
NIH K08AI148607
Novavax
Peds ID - Research Commitment
PSTP (Faculty Early Career Award)

Thanks to our study participants and maternity staff!
Questions?