IMmunization to Protect African Children from Transmission of Hepatitis B (IMPACT-B study)

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on behalf of IMPACT-B study team
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Background

- WHO elimination targets aim for <0.1% HBsAg prevalence in children by 2030

- Current 5 year old HBsAg prevalence is 2.5% in Africa

- HBV mother-to-child transmission (MTCT) is now the major mode of residual HBV transmission

- In the African region, coverage of HBV MTCT interventions is low

Nayagam et al, Lancet Infectious Diseases 2016
Low coverage of HepB-BD in Africa

- Challenges to timely HepB-BD including:
  - Difficult to administer in rural settings or where out-of-facility births are high
  - Lack of funding support
  - Lack of awareness about importance of HepB-BD

- Most data on HepB-BD effectiveness is from Asia & North America
  - In Africa, one controlled study Ekra et al (HepB-BD and HepB3 groups)
    - no significant difference in MTCT rates overall
    - high rates of failure amongst HBeAg positive mothers

Polaris Observatory Collaborators, Lancet Gastro Hep 2018
Impact of HepB-BD scale-up

Global 5-year-old prevalence

HBV-related deaths averted by region

➢ HepB-BD scale-up to WHO 90% coverage levels could avert 500,000 HBV-related deaths in Africa (for 2020-2030 birth cohorts).

De Villiers et al, Nature Comms 2021
IMPACT-B study

IMmunization to Protect African Children from Transmission of Hepatitis B
Multi-centre: Senegal, The Gambia, Ethiopia
Duration: 30 months

• Overall study aims
  – To furnish important data gaps in Africa on effectiveness of timely HepB-BD stratified by HBeAg/HBV viral load status.
  – To allow better quantification of the impact of scaling up HepB-BD and therefore guide policies on HepB-BD introduction and scale-up in the region.
IMPACT-B Study Team

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• University of Oslo, Norway
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Overall study approach

Comparison of HBV MTCT risk in children (at 9 months of age) born to HBsAg positive mothers who receive timely HepB-BD and those who do not.

- **West Africa (Senegal + The Gambia)**
  - Comparison of outcomes in children who receive HepB-BD and those who don’t as part of **routine immunization policy**
  - **Prospective** methodology

- **East Africa (Ethiopia)**
  - Comparison of outcomes in children born in MoH HepB-BD **pilot sites vs non pilot** ‘control’ sites
  - **Retrospective** methodology
Primary Research Objectives

To evaluate the effectiveness of timely HepB-BD

- with respect to maternal HBsAg status (*i.e.* overall effectiveness)

- with respect to key indicators for increased transmission risk: maternal HBeAg status and level of HBV DNA
Secondary Research Objectives

- To assess the proportion of pregnant women at high risk of HBV MTCT in the study countries (defined as positive HBeAg and/or HBV DNA ≥200,000 IU/ml)

- To estimate the absolute risk of HBV MTCT with and without TBD
  - amongst babies born to HBsAg positive mothers (overall)
  - with respect to maternal HBeAg status and level of HBV DNA.

- To determine the proportion of infants that receive a) TBD vaccination (ie within 24 hours of birth) and b) complete hepatitis B vaccination series, and evaluate factors related to newborns and infants not receiving TBD and infant vaccination.
**Study methodology**

**West Africa**

- **Pregnant women attending antenatal services in selected study sites**
  - Antenatal services
    - **n = 8500 pregnant women in each study country**
  - HBV birth dose vaccination (in addition to routine infant vaccination as part of national policy)
  - HBsAg rapid Point-of-Care test (result given on site)
    - Positive Test
      - Sociodemographic information
      - Serum + DBS (for HBeAg serology and HBV DNA to be done retrospectively)
    - Negative Test
      - HBV birth dose vaccination (in addition to routine infant vaccination as part of national policy)
  - Infants aged 9 months:
    - Dried Blood Spot for HBeAg serology
    - Review of vaccination records & structured questionnaires

**Ethiopia**

- **Women giving birth at selected sites**
  - "Pilot Hospital" where HepB-BD is routine
    - HBV positive mothers traced postpartum and invited for testing
      - N=130
        - Infants tested with HBsAg
          - Mothers tested with HBV DNA, HBeAg and genotype
            - MTCT risk calculated:
              - (infected infants) / (HBV positive mothers)
              - Effect estimate of HepB-BD
                - $1 - (\text{MTCT risk with HepB-BD} / \text{MTCT risk without HepB-BD})$
  - "Control Hospital" where HepB-BD is NOT routine
    - HBV positive mothers traced postpartum and invited for testing
      - N=130
        - Infants tested with HBsAg
          - Mothers tested with HBV DNA, HBeAg and genotype

*Ethiopia sample size = 260 HBsAg +ve mothers*
i) MTCT risk at age of 9 months will be determined for each of the following groups based on whether they received TBD or not and HBeAg/HBV VL status of mother

<table>
<thead>
<tr>
<th>TBD and HBeAg status</th>
<th>TBD and Viral load status*</th>
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</thead>
<tbody>
<tr>
<td>Group A = no TBD, HBeAg +ve</td>
<td>Group 1 = no TBD, High VL</td>
</tr>
<tr>
<td>Group B = no TBD, HBeAg –ve</td>
<td>Group 2 = no TBD, Low VL</td>
</tr>
<tr>
<td>Group C = TBD, HBeAg +ve</td>
<td>Group 3 = TBD, High VL</td>
</tr>
<tr>
<td>Group D = TBD, HBeAg-ve</td>
<td>Group 4 = TBD, Low VL</td>
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</tbody>
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ii) Effectiveness of HepB-BD will be determined as follows

| Overall Effectiveness (all HBsAg positive women) | = Group A&B vs Group C&D |
| Effectiveness in HBeAg positive women            | = Group A vs Group C    |
| Effectiveness in HBeAg negative women            | = Group B vs Group D    |
| Effectiveness in High VL women                   | = Group 1 vs Group 3    |
| Effectiveness in Low VL women                    | = Group 2 vs Group 4    |
Summary

• Reducing HBV MTCT is an urgent public health priority globally and in Africa

• Narrow window of opportunity to answer an important question of HepB-BD effectiveness in Africa

• We hope that this collaborative study could contribute to increasing the evidence base and inform decisions about HepB-BD scale-up in the region