Development of WHO Guidelines for the Prevention of Mother-to-Child Transmission of Hepatitis B Virus Infection

Guidelines Development Group Meeting
9 – 10 September 2019
Room - D46025 (4th Floor, D Building)
Geneva, Switzerland

CONCEPT NOTE

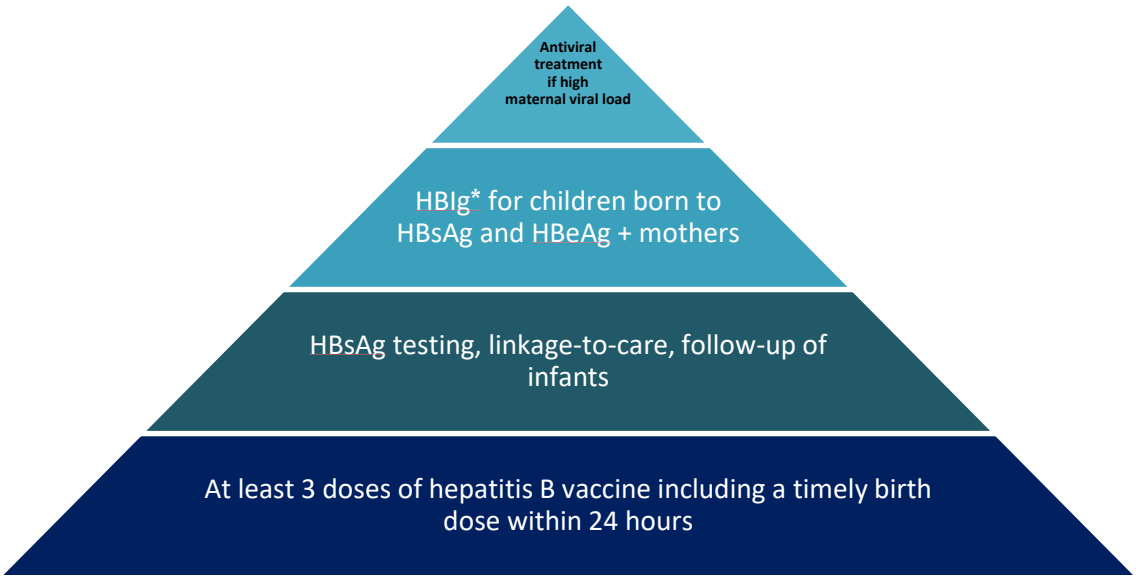
Background

WHO estimated that in 2015, 257 million people were living with chronic Hepatitis B Virus (HBV) infection worldwide, placing them at risk of serious illness and death from cirrhosis and hepatocellular carcinoma (HCC). In May 2016, the World Health Assembly endorsed the Global Health Sector Strategy (GHSS) on viral hepatitis, which proposes the elimination of viral hepatitis as a public health threat by 2030. Elimination is defined as a 90% reduction in incidence and a 65% reduction in mortality of viral hepatitis. To reach the HBV incidence impact target by 2030, Hepatitis B surface antigen (HBsAg) prevalence in children five years of age should fall below 0.1%, with an interim HBsAg prevalence target of 1% by 2020 in this age group.

To reduce the incidence of HBV infection, WHO has recommended inclusion of the hepatitis B vaccine (including the birth dose) in the Expanded Programme of Immunization since 1992. The birth dose of hepatitis B vaccine constitutes post-exposure prophylaxis to prevent vertical transmission of infection to infants exposed to HBV during childbirth and initiates immunization for lifelong protection against HBV infection. The three dose HBV vaccination series, including a timely birth dose, is the foundation on which other interventions to reduce perinatal transmission can be built (see Figure 1).

Perinatal transmission of HBV infection is the most common form of transmission in high prevalence regions. A proportion of infants born to HBsAg and Hepatitis B e antigen (HBeAg) positive mothers will still become infected despite HBV vaccination and Hepatitis B immune globulins (HBIg) prophylaxis. Estimates of the risk of transmission, vary, but are related to maternal viral load levels. Very high maternal concentrations of HBV DNA, typically observed in HBeAg-positive women, confer an elevated risk of transmission (ranging from 20% in Africa to 32% in Asia), despite HBIg and vaccine prophylaxis.

Figure 1. Incremental approach to prevention of HBV infection at birth and in the first years of life.



*HBIG may be of additional benefit for newborn infants whose mothers are HBeAg-positive.

In 2015, WHO issued its prevention, care and treatment guidelines of persons with chronic HBV infection. These guidelines include recommendations to treat HBV-monoinfected eligible, pregnant women with tenofovir for their own health. However, no recommendation was made on the routine use of antiviral therapy to prevent HBV mother-to-child transmission. The 2015 Guidelines Development Group (GDG) recognized that a proportion of infants born to HBV-infected mothers acquire HBV infection despite prophylaxis and WHO commissioned an evidence review to assess the clinical and economical evidence for the effectiveness of antiviral therapy during the third trimester of pregnancy to reduce maternal transmission of HBV infection. The results suggested that maternal treatment with antivirals during the third trimester of pregnancy may be clinically effective and cost-effective in helping to further reduce vertical transmission of HBV infection. However, the review had its limitations and there was a lack of consensus as to the programmatic implications, given the regional differences in timely birth dose uptake and access to testing and treatment. The 2015 GDG, therefore concluded that a formal recommendation could not be made at the time. Since the publication of the WHO 2015 HBV guidelines, new evidence has become available. WHO has also received requests for updated guidance from several regions, and to achieve the WHO HBV elimination goals, treatment of pregnant women with high HBV DNA viral load with antiviral therapy may need to be recommended in addition to three dose infant vaccination (including a timely birth dose). In view of this, WHO is updating its guidelines to include recommendations on the prevention of HBV mother-to-child transmission.

A Guidelines Development Group (GDG) has been identified, Person, Intervention, Comparison, Outcome (PICO) questions drafted, and a proposal was approved by the Guidelines Review Committee. As a part of this process, a two-day Guidelines Development Group (GDG) meeting will be held on 9-10 September 2019 in Geneva.

Objectives of the guidelines

The overall objective is to provide evidence-based guidance on the use of antiviral medicines in pregnant women for prevention of HBV mother-to-child transmission. The guideline is expected to provide the basis and rationale for the development of national guidelines on the management of mother-to-child transmission of HBV with the aim of reducing the global burden of HBV infection, in line with the viral hepatitis elimination goals.

The specific objectives of the guidelines updates are to:

- provide an updated evidence summary, GRADE review, evaluation of the risk-benefit analyses, assessments of feasibility, costs and cost-effectiveness and acceptability of the proposed recommendation;
- provide a recommendation on the use of antiviral medicines in pregnant women for the prevention of HBV mother-to-child transmission in the context of different programmatic scenario;
- identify considerations and tools that could support the implementation of the proposed recommendation at country level;
- Describe a monitoring and evaluation framework;
- identify research gaps.

Scope of the review and meeting

A range of evidence, assessments and evaluations will be made available to the GDG in order to review, suggest revisions and approve the final recommendations during the final consensus meeting.

Two systematic reviews have been commissioned from the Institute Pasteur with lead investigator, Yusuke Shimakawa. These reviews are structured according to the PICO scheme. In addition, modelling will be performed by Imperial College, led by Shevanthi Nayagam.

Outputs from the GDG meeting

Expected outputs of the Guideline Consensus Meeting are:

- finalized decision-making tables and consensus on recommendations including a synthesis of harms and benefits, acceptability, and resource considerations;
- identification of implementation steps and tools required;
- identification of research gaps and needs, as well as other issues requiring urgent attention.