

## MATERNAL AND FOETAL PROGNOSIS IN WOMEN WITH HEPATITIS B INFECTION

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**Abstract:** *These instructions are formulated for presenting the template used for editing the articles for the scientific journal Bulletin of the Transilvania University of Braşov. The material presents the camera ready form of the articles. The abstract should synthetically outline all the pertinent results, in a short but intelligible form. The abstract should begin through clearly stating the purpose of the paper and should end by formulating the most important conclusions. There will be used short, direct and complete sentences, written in a single paragraph, without "tab"-s. The abstract will have 7...10 lines.*

**Key words:** *pregnancy, hepatitis B infection, prognosis.*

### 1. Introduction

The infection with hepatitis B virus (HBV) is the main cause of viral acute hepatitis around the world. HBV infection can be asymptomatic or it can be associated with severe symptoms of acute hepatitis. It has been estimated that 40% of world's population has either been exposed or has the chronic form of hepatitis B infection. This is the equivalent of 350 millions HBV carriers around the world. Therefore, the HBV is one of the most infectious diseases in the world. Almost a million people die every year due to HBV.

The prevalence of HBV considerably varies from 0.1% and 20% in different parts of the world. The areas with low prevalence (0.1-2%) are in Western Europe (showing consistent differences within the continent), United States, Canada, Australia, and New Zealand; the areas with

medium prevalence (3-5%) are the Mediterranean countries, Japan, Central Asia, the Middle East, Latin and Central America; the areas with high prevalence (10-20%) are in the Southern Saharian Africa, Southern Asia and China. This diversity could be the effect of exposure and infection at different ages. The age of infection is connected with risk of becoming chronic. The progression rate of HBV from the acute form to chronic form decreases with the age, being of 90% in the case of perinatal infection and approximately 5% or less in adults. (Stevens 1975; Wasley 2008).

Newborns from mothers tested positive for AgHBs can be immunized actively or passively within 12 hours from birth. The immunization is very important because the vertical transmission of HBV could be reduced from 95% to 5% (Ranger-Rogez 2004). To the mothers with high viremia

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(over 50 millions UI/ml, antiviral therapy with inhibitors of HBV polymers can be additionally administered. If the immunization active/passive has been performed, the caesarian is not mandatory for birth. Mothers with vaccinated newborns may breast feed, except those who received oral antiviral medication which can be detected in maternal milk.

### **Pregnancy and type B hepatitis**

Viral hepatitis is the most frequent hepatic disease met in pregnant women. There are at least 5 distinct types of viral hepatitis. In all these forms, symptoms can precede jaundice with 1 or 2 weeks. (nausea, head aches, asthenia).

The type hepatitis named also until recently serum hepatitis, spread wide world is endemic in some regions such as Asia and Africa. The HBV infection is an important source for the chronic hepatitis, for hepatocellular carcinoma or hepatic cirrosis as well.

The evolution of the HBV infection is not influenced by pregnancy except perhaps the increase of premature births. The trans-placental transfer from mother to foetus rarely occurs. But the fetus' infection can occur by ingestion or by contact with contaminated materials, at birth. Part of the children are asymptomatic but some develop a supra-acute form and die.

From a chronic carrier mother of the virus can be usually prevented through administering immunoglobulin immediately after birth, promptly followed by vaccination. For these reasons, seric screening is recommended for all pregnant women during prenatal consults. If tested positive, especially if the e antigen has been detected, immunoglobulin and vaccination will be administered.

Active chronic hepatitis is a disease of diverse etiology followed by hepatic

necrosis, active inflammation, and fibrosis that lead to cirrhosis and hepatic insufficiency, in most cases due to the infection with the hepatitis B virus. Another source is autoimmune chronic hepatitis.

Classical features of the disease are insidious onset, over several weeks or months, intermittent fatigue, anorexia and persistent low-grade fever or persistent jaundice and the progression to cirrhosis is a rule.

The effects of pregnancy on chronic hepatitis and the effects of hepatitis on pregnancy depend largely on the existence of portal hypertension and liver failure.

Pregnancy is unusual when the disease is severe because anovulation is common. Corticosteroids have improved both fertility and survival in women with chronic autoimmune hepatitis

The frequency of fetal death and premature birth increases but not that of malformations.

The Remote prognosis of these women is reserved and they must be advised regarding abortion and sterilization.

Hepatitis B is found in approximately 1-2 in 1,000 pregnancies, of which about 0.5% -1.5% mothers are chronic carriers of HBV (HBsAg positive). HBV transmission from mother to fetus during pregnancy (at intrapartum frequently) is one of the most effective methods of transmission and spread of HBV usually teamed with long-term consequences such as liver cirrhosis or hepatocellular carcinoma. Transmission from mother to fetus may occur in four ways:

1. Transplacental (perhaps in rare cases)
2. Intrapartum
3. Postpartum
4. The breast milk or colostrum

Several clinical studies have shown that the predominant route of perinatal HBV transmission is intrapartum through exposure to infected blood, genital

secretions, or faeces. Approximately 80-90% of children whose mothers have hepatitis B virus during the 3rd quarter of pregnancy will become carriers of HBsAg. When HBV is contacted in early pregnancy, only 10% of cases will be transmitting the virus to the fetus.

There are biochemical values and histopathological abnormal aspects but usually these abnormalities are not severe. Also, most new-borns and children infected with hepatitis are asymptomatic or have minor clinical signs of disease. Despite these apparently undamaging clinical and biochemical the persistence of HBsAg may lead to chronic hepatitis or cirrhosis and even hepatic cirrosis.

Table nr 1.

Clinic status	Transmission rate
Ag HBs+, Ag Hbe-	10-20%
Ag HBs+, Ag Hbe+	90%
Acute Hepatitis, in 1 <sup>st</sup> trimester	10%
Acute Hepatitis, in 3 <sup>rd</sup> trimester	80-90%

#### Perinatal transmission of HBV

Clinical studies have shown that the crucial determinative of vertical transmission of HBV from mother to fetus, is the presence of antigen 'e'. HBeAg-positive mothers have a high viral load and are most likely to transmit the virus to newborns. Approximately 70% of newborns whose mothers were HBeAg positive were detected themselves with HBsAg positive until the 5th month of life.

In conclusion, almost all children born to HBeAg positive mothers became infected

with HBV during the first year of life, and about 85% of them became chronic carriers of HBsAg. Also, children whose mothers were HBsAg positive but HBeAg negative, can be infected with HBV and may develop a severe or even fatal acute hepatitis, but these are much more rare cases (about 5-10%). In the U.S. and most developed Western countries acute viral hepatitis is found in almost 10% of newborns from HBsAg carrier mothers

The greatest risk of developing acute viral hepatitis is in children born to mothers with HBsAg + HBeAg positive. The lowest risk of developing hepatitis are the children whose mothers have HBeAg antibodies.

#### Types of available vaccines

The first vaccine against hepatitis B have been plasmatic vaccines. They contain the HBV surface antigen, HBsAg, taken from plasma the carriers of the chronic virus and purified. Currently are used vaccines made by genetic engineering, Recombivax HB, Engerix, dosed in 2.5 mg (0.2 ml), 10 mg (0.5 ml) recently entered into obligatory vaccination of all newborns in our country.

Vaccination against hepatitis B virus offers protection for the hepatitis D virus disease as well. The protection is obtained by taking a series of three intramuscular doses of vaccine. Two schemes can be recommended for primary immunization: a rapid schedule, with doses at 0, 1 and 2 months, which will give faster installed protection, schemes that allow more time between the second and third dose, at 0, 1 and 6 months. The latter takes longer, but induces higher antibody titers. It is considered an effective antibody titer of over 10miliU.I./ml.

The vaccine must be administered in muscle and not fat tissue in the deltoid region in adults and in the anterolateral thigh for infants. Antibody titers tend to be

lower when the vaccine is administered into the fatty tissue of buttock region. Subcutaneous administration is indicated only in patients with severe bleeding tendency, such as hemophiliacs.

After immunization with 0, 1, 2 months scheme, is recommended that a booster at 12 months after the first dose. The next booster is not needed for at least eight years. After the schedule 0, 1, 6 months is recommended five years booster after the first vaccination. The vaccine protects against hepatitis B and hepatitis D virus infection. By preventing infection the prevention of liver cirrhosis and liver cancer is ensured, two severe diseases of uncertain prognosis.

#### **Study on maternal-fetal prognosis and characteristics of hepatitis B in pregnancy**

The study was based on data obtained from case report forms of patients admitted during 2008-2009, and infants enrolled in the Obstetrics and Gynecology 'I. A. Sbârcea' Braşov in the same period.

In 2008 it has been recorded a total of 4593 deliveries of which 1364 births by cesarean delivery, representing 30% of all births. In 2009 the total number of births was 4737, of which 1592 were by cesarean delivery, i.e. 34% of births. Of the total analyzed births were identified 12 cases of pregnancy associated with viral hepatitis B in 2008, representing approximately 0.26% of all births registered in the same year, and 15 cases in 2009 representing 0.31% of total births. Of these 27 deliveries made in the analysis were 18 births by cesarean delivery and 9 were natural births and caesarean sections 4 and 8 natural births in 2008, and 10 caesarean sections and natural births in May 2009.

Analyzing the demographic and social aspects of patients' in their level of training was concluded that most patients come

from urban areas, have an average level of education and are aged between 20 and 38 years.

Table nr 2.

Year	Number of cases of pregnant women with HBsAg +	Number of births by caesarean section	The number of natural births	Total births	Percent
2008	12	8	4	4593	0,26%
2009	15	10	5	4737	0,31%

In terms of parity and period of pregnancy, following data were identified:

Table nr 3.

Parity	Number of cases
primipare	17 parturient
secundipare	9 parturient
tertipare	0 parturient

Related to pregnancy was found in 27 births analyzed, 22 were term births 39-40 weeks respectively, and 5 were premature births at 33 and 34 weeks of pregnancy. It was identified only one pregnancy of twins.

Analyzing biochemical and serological data from observation sheets was concluded that all 27 cases of pregnancy associated with hepatitis B patients on admission had normal values of biochemical tests (blood count within normal limits, WBC and thrombocytes counts within normal limits and the transaminases normal values). Also, none of the pregnant women showed any clinical signs of illness at admission.

Of the 27 pregnant carriers of HBsAg, in the case of 8 patients the test reports revealed the absence of HBeAg, normal transaminases values during pregnancy, and recommendations of the medical

infectious diseases specialist on the end of the delivery, administrating immunoglobulin in newborn and any vaccination schedule. To the remaining 19 pregnant carriers of HBsAg were not identified data about admissions in infectious diseases clinic during pregnancy or any recommendations or dosing of HBeAg.

History pregnancy shows that all pregnant women hospitalized in this period knew they were carriers of HBsAg. Also there were no hospitalizations for clinical signs of hepatitis B or changes in transaminases. The data obtained showed only few cases of admissions in the first trimester of pregnancy for dizgravidii emetizante, or imminent threat of miscarriage.

Among the indications for cesarean birth, besides the condition of HBsAg carriers were also identified: scared uterus, placenta praevia with bleeding, pelvic presentations from primiparous, pregnancy-induced hypertension, intrauterine growth restriction, bony pelvis narrow, col dystocia, myopia.

All 27 births resulted in live births, with weights ranging from 1650 to 4700 grams, Apgar scores between 8 and 10. There were a total of 6 preterm children of which two were premature Grade II, with weights between 1650 and 2100 grams who had seizures after birth transient apnea and acute respiratory distress syndrome after being Rebalance and having a favorable outcome.

There were no newborns identified with malformations, 2 children among those born prematurely was established prophylactic antibiotics for preterm ruptured membranes.

Of the 28 newborns from HBsAg + mothers were given hepatitis B immunoglobulin anti hepatitis B vaccine while only 11 babies and 4 of the newborn to 2 ml HEPATECT iv administrators

Table nr.4

Number of new-born	Administrati on of IgHB	Administration of Hepatect
28 n.n	11 n.n	4 n.n

Newborns had a favorable outcome, none presented during the maternity hospital clinical signs of acute hepatitis or biochemical values changed, being discharged with good general condition, some with transient physiologic jaundice, proper weight, artificial or mixed feeding recommendation , and making prevention of rickets and appropriate vaccination schemes.

### Conclusions

Limitation and correct performance of injectable treatments, transfusions, human albumin, gammaglobulin, virological control of donors, screening of pregnant women and hepatitis B vaccination in neonates during the first 24 hours after birth due to epidemiological risk area.

Vaccination is done in various schemes with vaccines: Engerix B, RECOMBIVAX HB GENHEVAC B, 10 micrograms intramuscularly 0-1-6 months, 0-1-2 months for infants of HBsAg positive mothers, 0-1-2-6 months for those with immune deficiency.

Specific anti-HBV immunoglobulins are useful in infants with accidental contamination HBs positive mothers' replicative phase. The dose is 0.05 to 0.07 ml. / kg.

Mother-child transmission risk is higher for HBV and it maintains at a low level even with vaccination at birth and is much lower in hepatitis HCV RNA in situations with high levels.

There is no evidence that HBV infection is a common infection in pregnancy. In developed countries with civilized people, the mortality rate of viral hepatitis is low. Where malnutrition is a problem there is a

higher mortality rate.

Incidence in spontaneous miscarriage in the first trimester of pregnancy in patients with acute hepatitis has increased, as it did the incidence of premature birth when hepatitis is contracted in the third quarter of pregnancy. However, the incidence of spontaneous abortions and premature births is higher in cases of infection with hepatitis than in other febrile illnesses.

Teratogenic risk of hepatitis B virus has not been proven.

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