Research Article

HBV-Infection and Pregnancy

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Abstract
To date, the problem of HBV-infection in pregnant women remains relevant and one of the most important for medical science and health care, as it can be considered as a maternal-fetal infection.
The aim of the research is to investigate the course of HBV-infection in pregnant women, depending on the duration of the disease, the degree of viremia and the activity of hepatitis, taking into account gestational periods.

Materials and methods. The course of pregnancy in 142 women aged 18-35 years with HBV-infection was monitored. Serum markers and viral load (VL) of hepatitis B (HB) were determined, as well as the levels of ALT, AST, thymol test, serum bilirubin levels during each trimester of pregnancy.

Results. In pregnant women with HBV-infection, HBsAg-carriage was most often diagnosed, and the replication stages were less frequent (96 and 46, respectively).
Clinical picture of the immune-active phase of chronic HBV-infection was oligosymptomatic without violation of pigment metabolism and manifestations of mesenchymal-inflammatory reaction. The minimal degree of cytolysis prevailed, which did not depend on the degree of the viremia. In women with immune-tolerant phase of cytolysis during pregnancy was not observed.
In pregnant women with replication stage of HBV-infection and low degree of viremia, the VL increased at 1-2 log compared to the second and third trimesters, and in women with high viremia – at 2-3 log.
In most women-carriers of HBsAg moderate degree of viremia predominated, and in the rest – it was not determined.
During the entire pregnancy, the immune-tolerant phase of chronic HBV-infection was latent and did not transform into the immune-active phase.

Conclusion. Thus, the diagnosis of chronic HBV-infection was verified before pregnancy in 2.8 %, and during pregnancy – in 97.2 % of women. Carriage of HBsAg prevailed in them (67.6 %), and replicative forms were registered in 32.4 % of patients. The peculiarity of replicative forms is subclinical (65.3 %) and asymptomatic (34.7 %) clinical course with low VL (? 105 copies/mL), which in most cases (91.3 %) increases before delivery at 1-2 log and is accompanied by low activity of hepatitis, without violation of pigment metabolism.

Keywords
HBV-infection; pregnant women

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Problem statement and analysis of the recent research

In recent years, viral hepatitis (VH) has become not only a great medical problem but also socio-economic one. According to various estimates, about 2 billion people in the world are infected with hepatitis B virus (HBV) and 300-450 million patients with chronic HBV (CHB), who are a constant source of infection [7, 8, 9].

In Ukraine, among the adult population, the average incidence of HBsAg carriers is 2.2 %, and the incidence of HBV infection in pregnant women exceeds 18 % [1, 2].

An important peculiarity of the age structure of patients with CHB in adults is its prevalence in young people of reproductive age (19-29 and 30-39 years), which promotes further activation of the sexual transmission of pathogen HBV, the growth of infection in pregnant women, more intense perinatal infection of newborns with HBV [6].

The problem of HBV-infection is one of the most urgent in modern medicine, as it is a frequent cause of chronic liver diseases in women of childbearing age. It is common for obstetricians, infectiologists, hepatologists, pediatricians, and therapists and requires the development of general strategy as for the pregnancy management in such women [3, 5].

According to the recommendations of WHO and the European Association for the Study of Liver, for women with HBV-infection who have not reached the stage of cirrhosis, as well as in the absence of signs of active inflammatory process in the liver or cholestasis, pregnancy is not contraindicated, since it does not have a negative effect on the course of CHB [1, 5]. The results of research in this area are somewhat controversial, however, most authors concluded that pregnancy does not affect the course of CHB [3, 5, 8, 9].

Because of the negative impact on the maternal and fetal health, the infection caused by HBV is a global medical and social problem in many countries of the modern world.
Therefore, knowledge of the natural course of HBV-infection in pregnant women is necessary to optimize the tactics of their management [3].

Objective of the study – is to investigate the course of HBV-infection in pregnant women, depending on the duration of the disease, the degree of viremia and the activity of hepatitis, taking into account gestational periods.

1. Materials and methods of the research

We monitored the pregnancy course in 142 women aged 18-35 years with HBV-infection. Serum markers of HB (HBsAg, anti-HBcIgM, anti-HBcIgG) were determined during women’s registering in antenatal clinic. In women with detected serological markers, HBV DNA was determined by polymerase chain reaction (PCR) – qualitative and quantitative (viral load (VL)) in the second and third trimesters of pregnancy. The activity of the inflammatory process in the liver by ALT, AST levels detection in blood serum during each trimester of pregnancy was monitored. The level of bilirubin and thymol test were also determined.

2. Results of research

The diagnosis of chronic HBV-infection has been verified in 142 pregnant women: before pregnancy in 4 (2.8 %), and during pregnancy – in 138 (97.2 %). Most often, the carriage of HBsAg was diagnosed as an integrative stage of the infection – in 96 (67.6 %) women, rarely the replication stage was detected in 46 (32.4 %) women, of which the immuneautoactive phase was in 14 (30.4 %), and the immunotolerant – in 32 (69.6 %) patients.

We did not observe any clinical manifestations of chronic HBV-infection in the replicative stage, except for increased fatigue in 16 (34.8 %) pregnant women and periodic discomfort in the right hypochondrium in 9 (19.6 %). Only in 5 (10.9 %) patients with the immuneautoactive phase hepatomegaly was detected without violation of pigment metabolism and manifestations of mesenchymal-inflammatory reaction (normal levels of bilirubin, thymol tests, absence of hypergammaglobulinemia).

In such women in 28.2 % of cases minimal, in 2.2 % – moderate degrees of cytolysis were observed, which did not depend on the degree of viremia. In the remaining 32 (69.6 %) women with immunotolerant phase of cytolysis during pregnancy was not observed.

In the dynamics, as a rule, before delivery, in women with a replicative stage of HBV-infection and low degree of viremia (VL < 10^3 copies/mL), VL increased at 1-2 log (91.3 %) compared with II and III trimesters, and in women with high viremia (VL = 10^3 copies/mL) – at 2-3 log (4.3 %). In 1 woman (2.2 %), the degree of viremia from boundary level (= 750 copies/mL) without cytolysis was transformed in the second trimester of pregnancy into moderate level (VL = 10^3 copies/mL) with a minimal activity level in III trimester. In one woman (2.2 %) on the contrary – viremia from moderate level in the second trimester (VL = 10^4 copies/mL) decreased to the boundary one with normal ALT level in III trimester.

In the majority of women (53.1 %), HBsAg carriage was accompanied by VL <10^4 copies/mL, and in 45 (46.9 %) it was not determined. During the entire pregnancy, the immunotolerant phase of chronic HBV-infection in women was latent and did not transform into the immunoactive phase.

3. Discussion

According to current research data, HBV-infection in pregnant women is usually asymptomatic, mainly in chronic form (97.4 %). The frequency of the integrative stage of the pathogen reproduction predominates over the replicative (79.1 versus 8.7 %). Their diagnostics in pregnant women is difficult, since both forms occur without jaundice and subjective manifestations of the disease, with the exception of the fact that replicative HBV-infection is characterized by asthenic (90-93 %) and dyspeptic (35-40 %) syndromes, hepatosplenomegaly (35-40 %), mesenchymal-inflammatory (32-36 %) and cholestatic syndromes (20-25 %), as well as minor liver function disorders, manifested by cytolysis syndrome in 50-52 % of patients, which coincides with our data [1, 5, 6, 8].

Concerning the cytolysis levels, the results of our study coincide with the authors’ research data, which indicate that in part of pregnant women (48-50 %), despite the replication of the virus, the level of ALT in serum can remain within the normal range throughout the pregnancy. At the same time, in HBsAg-positive pregnant women there were described cases that indicate on deterioration of the liver function even the development of fulminant hepatic failure [4, 5, 9].

According to some observations of other authors, during pregnancy in women with CHB thymol test increases, serum transaminases levels decrease against the background of normal levels of bilirubin and other biochemical indexes, amount of virus circulating in the blood decreases, which may be due to changes of immunological reactivity of the pregnant women organisms and increased plasma concentrations of estrogens [2, 6, 7, 8].

Perevertelen L. I. and co-authors (2014) indicate the intensive replication of the HBV in the first trimester of pregnancy, with a subsequent decrease in the level of viremia before childbirth (in the third trimester of pregnancy positive results of PCR were obtained in 28 % of women) [5]. Chuikova K. I. and co-authors (2011), by contrast, investigated the increase in the level of viral replication up to 36 weeks of gestation, which coincides with our study [6].

4. Prospects of further research

Prospects of further research will be aimed at study of the risk factors that contribute to perinatal infection of the fetus.

5. Conclusion

Thus, the diagnosis of chronic HBV-infection was verified before pregnancy in 2.8 %, and during pregnancy – in 97.2 %
Carriage of HBsAg prevailed in them (67.6%), and replicative forms were registered in 32.4% of patients. The peculiarity of replicative forms is subclinical (65.3%) and asymptomatic (34.7%) clinical course with low VL (< $10^5$ copies/mL), which in most cases (91.3%) increases before delivery at 1-2 log and is accompanied by low activity of hepatitis, without violation of pigment metabolism.

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