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Diagnosis of liver disorders in pregnant women with HBV Infection

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Abstract

Major indicators characterizing the functional state of the liver in pregnant women with hepatitis B are presented in the article. The level of main enzymes and proteins reflecting the liver disorders was examined in pregnant women with HBV infection including alanine aminotransferase, aspartate transaminase, gamma-glutamyltransferase, thymol test, total protein, effective concentration of albumin and albumin-globulin ratio for the prevention of perinatal complications and long-term effects of viral influence on the woman's liver in the future. Revealed abnormalities indicate the presence of endogenous intoxication, cytolysis and disorder of protein-synthesizing liver function.

Keywords: HBV infection, pregnant women, liver, gamma–glutamyltransferase.

1. Introduction

One of the most common infectious diseases causing significant negative impact on public health is hepatitis B virus. By prevalence of HBV infection Ukraine takes one of the first places in Europe. Thus, the incidence of disease is on average 32.5 per 100 thousand of population. Over the last 10-15 years there has been an increase in the overall incidence of HBV infection due to latent forms^[1, 2].

Asymptomatic forms of hepatitis were proven to be the most prone to chronization. According to WHO, more than 1/3 of the world's population is infected with hepatitis B virus and over 1 million people die from various clinical manifestations of the infection annually^[2].

Increased frequency of hepatitis B virus detection in pregnant women is of particular concern among obstetrician-gynecologists due to significant negative effect on pregnancy, childbirth, level of perinatal losses and vertical transmission of hepatitis B causative agent from mother to child^[3]. The pregnant women should be examined to detect HBsAg. However, when it is found, taken measures are aimed only at preventing the spread of infection, and clinical and biochemical examinations of women are not studied in dynamics enough considering the absence of subjective and objective signs of HBV infection. Insufficient attention is paid to early diagnosis of hepatobiliary disorders in pregnant women with hepatitis B^[3, 6].

Liver is known to play a major role in maintaining metabolic homeostasis in the body. HBV infection in pregnant women is accompanied by systemic manifestations of metabolic disorders. The liver has a large reserve property, so that slight and even moderate damage of its cells cannot significantly affect its metabolic functions^[3].

Biochemical functions in which the liver plays a major role include intermediate metabolism of amino acids and carbohydrates, and synthesis and breakdown of proteins and glycoproteins. Liver function tests are carried out to determine the nature and extent of violations of these biochemical functions in pregnant women. These tests are based on laboratory research methods showing the state of the body as a whole and characterize some of its functions or the integrity of structural elements.

2. Materials and methods

120 women were examined in the period of 28-40 weeks of pregnancy. They were divided into the following groups: I group included 80 pregnant women with HBV infection, II group comprised of relatively healthy pregnant women with uncomplicated pregnancies.

Clinical and biochemical indicators were determined in the blood serum of the pregnant woman in fasting state. They included thymol test, total protein, effective albumin concentration (EAC), albumin-globulin ratio (A/G ratio), alanine aminotransferase (ALT), aspartate transaminase (AST), gamma-glutamyl transferase (GGT).

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Aminotransferase activity and GGT that reflect the state of the cell membrane were determined to evaluate the cytological syndrome in examined patients. Unified dinitrophenylated method by Raytman-Frenkel was used in order to determine the activity of transaminase [4, 6]. This enzyme is more sensitive to liver cells disorders than ALT and AST. One part of enzyme is located in the cytoplasm; another is connected with the membranes of the microsomal fraction and biliary pole of hepatocytes which gives us an opportunity to refer GGT to enzymes that depend on membranes. Unified method with substrate gamma-glutamyl-n-nitroanilide lies in the fact that GGT catalyzes the transmission reaction of L-gamma-glutamyl residue from L- gamma-glutamyl-n-nitroanilide to glycylglycine. The amount of n-nitroaniline released during the reaction is a measure of activity of gamma-glutamyl transferase [4, 5].

Serum total protein was determined by biuret reaction; albumin in serum was defined by bromocresol green indicator. Scientists at SRI of Physical-Chemical Medicine of Ministry of Health of the Russian Federation offered fluorescent method to control the state of adhesive centers of albumin in serum or blood plasma [6]. The method is based on specific interaction of fluorescent organic dye K-35 with albumin in blood plasma. Depending on the conditions of the interaction intensity of dye fluorescence from plasma albumin displays various properties of albumin globule. This fluorescence intensity measured in grams per liter is also called "effective concentration of albumin".

Determination of serum protein fractions was performed by turbidity method in which the phosphate solutions of certain concentration are precipitated to form different blood serum protein fractions of a very shallow suspension. Conclusions about the concentration of protein in the examined material are based on the degree of solution turbidity (which is determined by photoelectric colorimeter).

Statistical analysis of the results was performed using the program Statistica 6.0. Mean value (M) and mean difference ($\pm m$) were calculated. Non-parametric Mann-Whitney test was used to compare two independent groups on one basis; Wilcoxon test was to compare two dependent groups. The difference was considered reliable at $p < 0.05$.

3. Results and discussion

Studying enzyme activity of blood serum in women with normal pregnancy we obtained the following results: ALT level in serum of healthy pregnant women was 0.4 ± 0.16 mcmol/h*ml, AST was within 0.2 ± 0.21 mcmol/h*ml that is they did not exceed the performance standards with the reliability $p < 0.05$. Aforementioned enzymes activity was slightly increased in physiological pregnancy, but their values were within the average values of enzyme activity in the blood of healthy non-pregnant women [7]. The level of GGT in the control group ranged from 17.12 ± 6.59 u/l corresponding to physiological standard. Thymol test of women in this group was 2.4 ± 1 at $p < 0.05$ within the physiological norm.

Moderate reduction of proteins, especially albumins, is characteristic of pregnancy, even physiological, which is explained by the fetus' needs [8]. Total protein level in women of the control group was within 70.6 ± 3.23 g/l, A/G ratio was 56.4/43.8%, and EAC was 36.4 ± 2.44 g/l.

Table 1: Comparative characteristics of indices of protein metabolism and enzyme function in pregnant women with HBV infection and physiological pregnancy ($M \pm m$)

Studied indices	Group I (n=80)	Group II (n=40)
Total protein, g/l	$60.9 \pm 3.37^{**}$	70.6 ± 3.23
EAC, g/l	$20.8 \pm 2.44^*$	36.4 ± 2.44
A/G ratio, %	50.3/45.2	56.4/43.8
Thymol test, S-H units	$5.8 \pm 2^{**}$	2.4 ± 1
ALT, mcmol/h*ml	$0.89 \pm 0.14^{**}$	0.4 ± 0.16
AST, mcmol/h*ml	$0.52 \pm 0.07^{**}$	0.2 ± 0.21
GGT, u/l	$58.79 \pm 15.8^{**}$	17.55 ± 6.59

Note:

- * – reliability ($p < 0.05$) compared with group II.
- ** – reliability ($p < 0.01$) compared with group II.

Protein metabolism indicators in women with hepatitis B were significantly larger than the standard indicators. Thymol test in group I was 5.8 ± 2 units which was 2.4 times higher than in women in group II, at reliability $p < 0.05$. Reduction in total protein by 13.4% was observed in pregnant women with HBV infection, A/G ratio was reduced by 10.8%, and EAC in women of the main group was reduced by 42.8%. Scientists' researches proved that both quantity and "quality" of albumin molecules is important as well as their ability to maintain oncotic blood pressure, to inversely bind and carry a variety of substances in the body, to participate in redox reactions and to support blood ion balance [7, 8]. Albumin has plastic functions; it interacts with proteases, affects the permeability of endothelial tissue, microcirculation, regulates apoptosis, cleanses the body of harmful toxins, free radicals and inflammatory mediators and others. Analyzing the data, changes in the ratio of blood protein composition were observed in women with HBV infection.

The study of enzyme activity in serum of pregnant with HBV infection revealed distinct indicators changes compared with the data of the control group which consisted of physiologically pregnant women. In such case a significant increase in transaminase activity was determined in 47.5% of pregnant women with HBV infection. As can be seen from Table 1, ALT indicators in women of group I were 2.23 times higher and AST indicators were 2.6 times higher than that of group II, with the reliability of $p < 0.05$. Traditionally, increased activity of ALT and AST is interpreted as a reflection of histochematic barrier breach or cytolysis activation.

GGT level was significantly higher in women with HBV infection compared to healthy pregnant women and was 3.35 times higher in women of group I than in women of control group with the reliability $p < 0.05$. Gamma-glutamyl transpeptidase was increased in 83.75% of women with HBV infection. Traditionally, increased activity of ALT and AST is interpreted as a reflection of histochematic barrier breach or cytolysis activation, and GGT increase is interpreted as the result of endotoxin toxic effect on the liver.

Thus, the regularity of enzyme activity changes may indicate the symptoms of cytological, hepatodepressive and mesenchymal-inflammatory syndromes, protein metabolism disorders in the anamnesis of pregnant women with HBV infection.

4. Conclusions

Hepatic dysfunction was observed during the detailed examination of pregnant women with HBV infection in comparison with a group of healthy pregnant women. Changes of indicators of protein-synthesizing liver function were detected, mainly hypoproteinemia with simultaneous hypergammaglobulinemia. Increase in thymol test level was also observed, indicating to dysproteinemia. All this indicates disorder of colloid blood stability and to a tendency of protein coagulation. Assessing liver enzymatic function increase in transaminase level was found indicating histochematic barrier breach with simultaneous cytolytic syndrome. Increase in the level of gamma-glutamyltransferase was observed in most examined pregnant women with hepatitis B signaling the presence of endogenous intoxication in women of this category. An examination of pregnant women with HBV infection detected significant abnormalities. Thus, detailed biochemical screening allows to begin adequate therapy, to prevent perinatal complications and the development of remote negative impact of the virus on the liver in the future.

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