ARTICLE

UDC 616.36-002.2:578.891:616-078

FEATURES OF COURSE OF CHRONIC VIRAL HEPATITIS B AND C IN PREGNANT WOMEN

[1]Abdikerimova M.M., [2]Anarbaeva J.A., [2]Shayimbetov A.T., [2]Suranbaeva G.S., [1]Abdikerimov M.M.

[1]Kyrgyz-Russian Slavic university named after B.N. Yeltsin, Bishkek, e-mail: myskalabdikerimova5@gmail.com;
[2]I.K. Akhunbaev Kyrgyz state medical academy, Bishkek, e-mail: jumagul.anarbaeva@mail.ru

The work shows the influence of pregnancy on the course of chronic viral hepatitis B and C: a) in pregnant women with CH, high activity of the infectious process was detected in 27.5% and low activity in 72.6%; in 35.3% of pregnant women with CHC, high and 64.7% of pregnant women had low activity of the infectious process; b) in pregnant women, chronic hepatitis occurred in a manifest form in 33.3% of patients with HBV infection and in 47.0% with HCV infection; c) chronic viral hepatitis was not fatal and did not pose a risk to the life of the pregnant woman, but exacerbation of the disease occurred in 8.7% of cases with HBV infection and in 13.7% of cases with HCV infection. Exacerbations of chronic hepatitis often develop in the first half of pregnancy (69.2%) and after its completion. The severity of clinical and laboratory manifestations of CHB and CHC in pregnant women depending on the gestational age, i.e. tension of compensatory and adaptive mechanisms with increasing gestational age. Assessing the overall effect of pregnancy on the course of chronic viral hepatitis, we found: – in most cases, pregnancy does not significantly affect the course of the disease and does not pose a risk to the life of the pregnant woman.

Keywords: chronic viral hepatitis B and C, pregnancy, trimester, gestational process, viral load, clinical and biochemical manifestations, manifest forms, subclinical forms

Introduction

Viral hepatitis B and C have acquired global distribution, while Kyrgyzstan belongs to regions especially disadvantaged with a steady tendency to spread due to the clinical manifestation of chronic hepatitis B virus (HBV) among residents [1, 2] infected before the introduction of preventive vaccination, and the uncontrolled situation with hepatitis C with its long-term period of subclinical currents [3, 4]. The increase in the incidence of hemocontact viral hepatitis among people of reproductive age creates prerequisites for the involvement of pregnant women in the epidemic process [5, 6]. According to numerous studies, chronic hepatitis (CH) has occupied one of the leading places in the structure of extragenital pathology in pregnant women in recent years [7].

Therefore, practical healthcare and scientific medicine face the problem of assessing the impact of the infectious process caused by hepatitis B (HBV) and C (HCV) viruses on the course of pregnancy, childbirth and the postpartum period, as well as the effect of pregnancy on the course of viral hepatitis [8]. There are reports in the available literature on the study of the effect of acute hepatitis B, C and E on the course of pregnancy and childbirth [9].

The purpose of the study – to study the features of the course of chronic viral hepatitis B and C in pregnant women.

Materials and methods of research

We examined 120 pregnant women suffering from chronic viral hepatitis B and C (CHB and CHC), who were divided into two groups. The main groups are 69 pregnant women with HBV and 51 pregnant women with HCV. 57 healthy pregnant women without liver pathology were examined as a control group.

Clinical data and biochemical parameters of liver function were evaluated in all patients. The laboratory examination included traditional general clinical methods: general blood and urine analysis, biochemical blood analysis (total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltranspeptidase (GGT), cholesterol, alkaline phosphatase, total protein and fractions, glucose). The diagnosis of viral hepatitis was confirmed by the identification of specific markers (HBsAg, HBeAg, anti-HCV IgM and IgG, DNA-HBV, total anti-HCV, RNA-HCV) by ELISA and PCR methods. The HCV genotype was determined in 51 pregnant women with HCV. Instrumental research methods included ultrasound examination of internal organs, fetus and fetometry in the second and third trimesters, Dopplerometry (Sono Scape S6 Pro Basic, China).

The statistical analysis of the obtained materials was carried out using the Statistica 6.0 program (StatSoft). The statistical analysis

consisted in calculating the arithmetic mean (M), its standard deviation (σ), as well as the standard error of the mean (m). The criterion of statistical reliability (p) was considered to be the value generally accepted in medicine.

Results of the research and discussions

69 pregnant women with HBV, 51 pregnant women with HCV and 57 pregnant women without liver disease (healthy) aged 19 to 30 years were under observation. Data on the distribution of women by age composition are shown in Table 1. As can be seen from Table 1, most women became pregnant at the age of 19-25 years, and under the age of 19, pregnancy occurred only in 9.0% of cases. The main age group of pregnant women is 19-25 years old. In the age group under 19, pregnant women suffering from chronic hepatitis C were more common, which, we believe, indicates parenteral infection, while, as is known, the hepatitis B virus is more often transmitted by household means.

Anamnesis of the disease in pregnant women suffering from CHB revealed that only 14 out of 69 patients (20.3%) were diagnosed with chronic hepatitis before the present pregnancy, they indicated a history of acute hepatitis, in 10 patients the disease was protracted. Among pregnant women suffering from CHC, only 4 out of 51 patients (7.8%) indicated acute hepatitis.

Consequently, in general, out of 120 pregnant women suffering from chronic viral hepatitis, only 18 patients had an indication of acute hepatitis (15.0%), and in 85.0% of cases it was "primarily chronic", but with varying frequency depending on the etiological factor. We believe that these indicators reflect the peculiarities of the nature of the infectious process.

Viral hepatitis C is a typical hemocontact infection, in 90% of cases it refers to post-transfusion hepatitis. When studying the epidemiological history of pregnant women with CHC, it was found that the artificial pathway of infection is 90.2%, while 76.5% is associated with surgical and dental care, and only 11.4% is associated with transfusion of blood components (Table 1). At that time, as is known, HBV is more often transmitted by household means: intrafamily contact (23.2%) and an unexplained transmission path (13.0%).

The correct assessment of the liver condition and the degree of its damage in patients with chronic viral hepatitis is of paramount importance for the organization of adequate therapy. To do this, 120 pregnant women suffering from chronic viral hepatitis were examined using ultrasound, and 35 practically healthy pregnant women were examined as controls. Ultrasound was performed mainly in the 2nd and 3rd trimesters. As a result of the research, it was found that 70 out of 120 pregnant women (58.3%) showed signs of chronic liver damage, 23 women (19.2%) showed biliary dyskinesia, while out of 35 pregnant women who did not suffer from pathology of the hepatobiliary system, according to clinical and laboratory data, two had changes, the characteristic signs of biliary dyskinesia.

To assess the replicative activity of hepatotropic viruses B and C in pregnant women, we examined 69 patients with CHB and 51 with CHC using PCR reflecting the natural replication of HBV DNA and HCV RNA. The conducted studies have shown (1st and 2nd trimesters of pregnancy): – among pregnant HBV patients, 19 out of 69 showed high (27.5%) and 50 low (72.5%) activity of the infectious process; – 18 out of 51 examined pregnant women with HCV showed high (35.3%) and 33 pregnant women (64.7%) showed low activity of the infectious process. The study of hepatitis C genotypes and serotypes revealed the predominance of genotypes 1b (51.0%) and 3ab (29.4), less often 2 (13.7%) and unidentified genotypes (5.9%).

Table 1

Distribution of pregnant women by age

Groups of women surveyed	Number of patients	Age in years					
		up to 19 years old		19-25 years old		30 years old and older	
		abs	%	abs	%	abs	%
Pregnant women with	(n=69)	4	5,8±	53	76,8	12	17,4
CHB	(n=51)	8	15,7	31	60,8	12	23,5
Pregnant women with	(n=57)	4	7,0	43	75,4	10	17,6
CHC	(n=177)	16	9,0	127	71,8	34	19,2

Table 2

The nature of clinical symptoms in pregnant women suffering from CH

Clinical symptoms	CHB (n= 69)		CHC (n= 51)		Healthy pregnant women (n= 57)	
	abs.	%	abs.	%	abs.	%
Weakness, fatigue	27	39,1	24	47,1	12	21,0
Heaviness in the right hypochondrium	18	26,1	21	37,3	-	-
Nausea and vomiting	13	18,8	15	29,4	4	7,0
Heartburn	4	5,8	6	11,8	-	-
Decreased appetite	12	17,4	12	23,5	-	-
Constipation	4	5,8	4	7,8	1	1,8
Ictericity of sclera and skin	7	10,1	11	21,6	-	-
Skin itching	4	5,8	8	15,7	-	-
Telangiectasia	3	4,3	3	5,9	-	-
Arthralgia	2	2,9	9	17,6		
Hemorrhagic syndrome	3	5,8	7	13,7		
Hepatomegaly of them: more than 2 cm 2 cm and less	18 5 13	26,1 7,2 18,8	20 9 11	39.2 17,6 21,6	-	-
Splenomegaly	2	4,3	5	9,8	-	-

During the examination of 120 pregnant women suffering from CH, it was found: – subclinical forms in 73 patients (60.8%), manifest forms in 47 patients (39.2%), of which 8 patients had jaundice (17.0%) and 39 (83.0%) in non–jaundice variants.

When analyzing the clinical picture in the examined pregnant women suffering from CH, as well as in the control group (in pregnant women who do not suffer from pathology of the hepatobiliary system) throughout the gestation period, among the subjective manifestations, we focused on the presence of symptoms of viral liver damage. In pregnant patients with CHC, the most common symptoms in all variants of chronic hepatitis in pregnant women were general weakness, fatigue, decreased appetite, nausea, pain and severity in the right hypochondrium of subicteric sclera and skin, itching, arthralgia, hepatomegaly and splenomegaly (Table 2). Pathological changes were significantly more often detected in patients with HCV than in CHC ($p<0.05$), which we associate with the predominant infection of this group of patients by hemocantact, while according to the literature, HBV infection occurs in 60-65% of cases with household contact. However, at the same time, in chronic hepatitis C, arthropathies in the form of arthralgias and arthritis are statistically significantly more common (17.6%), mainly in the form of oligoarthritis of the knee joints ($p<0.05$). Joint damage is explained by extrahepatic manifestations of the infectious process. Splenomegaly was detected twice as often in the same group of patients (4.3% in pregnant women with CHB and 9.8 with CHC, $p<0.05$), which is associated, as we believe, with a longer period of the infectious process.

In pregnant women who do not suffer from pathology of the hepatobiliary system, due to the presence of clinical manifestations of early toxicosis, unexpressed general weakness, nausea, and sometimes vomiting were observed. Clinical symptoms characteristic of women with chronic viral hepatitis were not detected in them.

Thus, analyzing the clinical symptoms in pregnant women suffering from chronic viral hepatitis B and C, we came to the conclusion that the gestational period was more difficult for patients with viral hepatitis C.

In pregnant women, the frequency of the manifest form of hepatitis increased with increasing gestation period and was observed mainly at 30-31 weeks of pregnancy, which is known to be a characteristic manifestation of pregnancy: with increasing gestation period, a strain on a woman's functional reserves is created even with a physiologically proceeding pregnancy [10]. The presence of pathology of such an important organ as the liver, which is involved in five hundred functions of the body,

contributes to the depletion of compensatory and adaptive capabilities [11].

During laboratory examination of pregnant women with chronic viral hepatitis B and C, we found that with increasing gestation period, there are deviations of biochemical parameters from the normal values shown in Table 3. As can be seen from table 3, with the development of the gestational process, the level of bilirubin gradually increases in pregnant women with CH, compared with the control group. In 85.5% of pregnant women with CHB and in 74.5% of pregnant women with CHC, the bilirubin level remained within the normal range during the first and second trimesters of pregnancy, only in 14.5% of patients with CHB and in 25.5% of patients with CHC, this indicator slightly exceeded normal values. In the dynamics of the gestational process, bilirubin levels increased by the third trimester in most pregnant women with CH (69.2%), and exceeded similar indicators of the control group by 1.7 times ($p<0.05$). An increase in the level of total bilirubin was observed in the group of pregnant women with CHC (72.5%), (95% CI (8.3-30.4)) 1.1 times compared with CHB (95% CI (8.4-26.8)) and 1.8 times with healthy pregnant women (95% CI (7.8-17.8)), ($p<0.05$). During gestation, cytolytic syndrome (increased ALT) was also detected in pregnant women with CH. The frequency of ALT elevation was significantly higher in the first trimester in 56.8% of patients with CHC (95% CI (97.8,-107)) than in 34.8% of pregnant women with CHB (95% CI (63.2-84.4)) and compared with healthy pregnant women (95% CI (24.7-39.5)), ($p<0.001$). The ALT level was more significantly higher in all trimesters in pregnant women with CHC (in the first trimester -1.4 times; II-1.5 and III-1.4 times) than in pregnant women with CHB ($p<0.05$).

Table 3

Biochemical parameters in pregnant women with HBV and HCV (M±m)

Indicators	Trimesters	CHB	CHC	Healthy pregnant women	
ALT (units/l)	I	73,8±5,3	102,7±2,3	32,1±3,7	$P_{1-2}<0,001$; $P_{1-3}<0,001$
	II	61,5±5,8	93,7±3,4	28,4±5,9	$P_{1-2}<0,001$; $P_{1-3}<0,001$
	III	47,3±6,0	66,8±4,3	23,6±5,6	$P_{1-2}<0,05$; $P_{1-3}<0,01$
Total bilirubin (mmol/l)	I	17,6±4,6	19,4±5,5	12,8±2,5	$P_{1-2}.>0,05$; $P_{1-3}>0,05$
	II	19,3±4,7	20,5±5,6	13,7±2,6	$P_{1-2}>0,05$; $P_{1-3}<0,05$
	III	23,6±5,1	25,7±6,1	14,2±2,6	$P_{1-2}>0,05$; $P_{1-3}<0,05$
Thymol sample	I	5,4±0,4	6,5±0,8	2,8±0,04	$P_{1-2}>0,05$; $P_{1-3}<0,001$
	II	5,6+0,5	6,4+0,9	2,5±0,03	$P_{1-2}>0,05$; $P_{1-3}<0,001$
	III	5,7+0,5	6,6±1,1	1,9±0,02	$P_{1-2}>0,05$; $P_{1-3}<0,001$
Total protein (g/l)	I	64,2±5,7	63,1±6,7	68,2±6,1	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	II	64,1 ±5,7	62,8±6,7	68,5±6,2	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	III	63,4±5,8	62,2±6,8	65,4±6,3	$P_{1-2}.>0,05$; $P_{1-3}>0,05$
Albumin	I	54,6±5,9	54,3±6,9	58,2±6,5	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	II	54,3±5,9	53,9±6,9	57,6±6,5	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	III	54,1±5,9	53,2±6,9	56,6±6,6	$P_{1-2}>0,05$; $P_{1-3}>0,05$
Alkaline phosphatase (units/l)	I	92,6±3,1	93,4±3,4	82,9 ± 4,9	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	II	105,3±	107,8±4,0	98,8 ± 1,4	$P_{1-2}>0,05$; $P_{1-3}<0,05$
	III	137,8±0,01	143,1±0,01	120,1 ± 0,01	$P_{1-2}>0,05$; $P_{1-3}<0,05$
GGT (units/l)	I	41,7±5,9	43,6 ±6,9	37,5±6,4	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	II	48,4±6,0	52,2±7,0	43,4±6,5	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	III	56,5±5,9	64,9±6,6	47,6±6,6	$P_{1-2}>0,05$; $P_{1-3}>0,05$
Cholesterol (mmol/l)	I	5,18±0,06	5,48±0,05	5,09±0,52	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	II	5,33±0,06	5,81±0,06	5,11±0,09	$P_{1-2}>0,05$; $P_{1-3}>0,05$
	III	6,28±	6,72±	5,32±0,49	$P_{1-2}>0,05$; $P_{1-3}<0,05$

With an increase in gestation period, a gradual decrease in ALT levels was also revealed in CHB (27.5%) and CHC (35.3%), but the most significant was in the third trimester in pregnant women with CHC (95% CI (58.2-75.4)), ($p<0.05$). A decrease in estrogen levels by the third trimester of pregnancy reduces the severity of the inflammatory process in the liver and helps to reduce the level of aminotransferases. The parameters of the thymol test in pregnant women with CHB and CHC were significantly higher than normal in the first trimester than in healthy pregnant women ($p<0.05$) and with the development of the gestational process, its indicators did not change significantly.

The study of the blood protein spectrum revealed a tendency to hypoproteinemia during gestation in pregnant women with CHB and CHC, due to a decrease in the level of albumins in the blood. These changes were more pronounced in pregnant women with CHC (95% CI (39.4-60.7)) in the third trimester of pregnancy than in CHB (95% CI (42.3-65.9)) and compared with healthy pregnant women (95% CI (43.4-69.8)), ($p>0.05$). The levels of alkaline phosphatase, GGT and cholesterol in pregnant HCV were significantly higher (68.6%) in the third trimester than in pregnant women with HBV (56.5%) and in healthy pregnant women (19.3%, $p<0.05$).

With an increase in gestation period in pregnant women with CHC, there was a decrease in the prothrombin index and fibrinogen by the third trimester (1.4 and 2.5 times, respectively) compared with relatively healthy pregnant women ($p>0.05$).

Laboratory examination of pregnant women with CH revealed exacerbations of chronic viral hepatitis in 6 out of 69 pregnant women (8.7%) with HBV-infections, in 7 out of 51 pregnant women (13.7%) with HCV infection. Exacerbations in pregnant women were easy in the non-jaundiced version, which means that the average values of the main biochemical parameters in

pregnant women with CHB and CHC significantly exceeded those of healthy pregnant women. Exacerbations of chronic hepatitis are more likely to develop in the first half of pregnancy – in 9 out of 13 women (69.2%) and after its completion.

Thus, the above data indicate the tension of compensatory and adaptive mechanisms in pregnant women with HBV and HCV with the progression of gestation period.

Conclusions

1. The severity of clinical and laboratory manifestations of CHB and CHC in pregnant women depends on the gestation period, i.e. the tension of compensatory and adaptive mechanisms with an increase in gestation period.

2. Exacerbation of the disease occurred in 8.7% of cases with CHB infection and in 13.7% of cases with CHC infection. Exacerbations of chronic hepatitis are more likely to develop in the first half of pregnancy (69.2%) and after its completion.

3. Assessing the overall effect of pregnancy on the course of chronic viral hepatitis, we found: in most cases, pregnancy does not significantly affect the course of the disease and does not pose a risk to the life of the pregnant woman.

References

1. Saryglar A.A., Dongak S.O., Ibragimova A.D., Novak K.E., Esaulenko E.V. Clinical and epidemiological characteristics of chronic hepatitis C in the Republic of Tyva // Journal of Infectology. 2023. Vol. 15, № 1. P. 55-60. DOI: 10.22625/2072-6732-2023-15-1-55-60.

2. World Health Organization. World Hepatitis Day 2019 [Electronic resource]. Available from: https://www.who.int/ru/campaigns/world-hepatitis-day/2019 (date of access: 15.05.2024).

3. Suranbaeva G.S., Alisherova A.Sh., Anarbaeva J.A. et al. Application of the MELD scale to assess the severity of liver cirrhosis in the outcome of chronic hepatitis C in the Kyrgyz republic // European Journal of Natural History. 2022. No. 6. P. 8-12. DOI: 10.17513/ejnh.34297.

4. Kanabekova A.K., Abdikerimova M.M., Abdikerimov M.M., Zholdoshev S.T. Variants of the course and outcomes of chronic hepatitis C and cirrhosis of the liver in their natural course // Sanitary doctor. 2018. Vol. 1. P. 32-38.

5. Baranovskaya E.I., Znovets T.V., Zhavoronok S.V. Pregnancy in women with viral hepatitis C // Russian bulletin of the obstetrician-gynecologist. 2019. Vol. 19, № 5. P. 38-42. DOI: 10.17116/rosakush20191905138.

6. Zaitsev I.A. Viral hepatitis in women of reproductive age // Current infectology. 2017. Vol. 5, № 3. P. 123-128.

7. Hou J, Cui F. Management Algorithm for Interrupting Mother-to-Child Transmission of Hepatitis B // Virus Clinical Gastroenterology and Hematology. 2019. Vol. 17. No. 10. P. 1929-1936.

8. Bragina T.V., Petrov Yu.A., Spiridenko G.Yu. Features of the course of pregnancy, childbirth and perinatal outcomes in women with viral hepatitis C // Medico-pharmaceutical journal "Pulse". 2021. Vol. 23. № 8. P. 14-20. DOI: 10.26787/nydha-2686-6838-2021-23-8-14-20.

9. Moses K.B., Moses V.G., Zakharov I.S., Elgina S.I., Rudaeva E.V. Hepatitis C during pregnancy – modern approaches to screening, treatment and prevention of complications // Mother and child in Kuzbass. 2019. Vol. 78, № 3. P. 4-9.

10. Chuikova K.I., Kovaleva T.A., Spivak S.V., Yakimov V.L., Minakova Yu.V., Petrova E.I. Clinical and biochemical manifestations in pregnant women with chronic viral hepatitis B and C in the third trimester and their relationship with the activity of the infectious process // Siberian Medical Journal. 2017. Vol. 32. № 4. P. 53-58. DOI: 10.29001/2073-8552-2017-32-4-53-58.

11. Filippovich O.M., Kuznetsov N.I. Features of the course of chronic viral hepatitis C in pregnant women // Kazan Medical Journal.2016. Vol. 97. № 5. P. 716-720.