Features of the clinical course of pregnancy, childbirth and the condition of newborns in women with HCV infection

K.V. Chaika, Yu.M. Zapopadna
Shupyk National Healthcare University of Ukraine, Kyiv

The objective: to conduct a retrospective clinical and statistical analysis of the pregnancy course, childbirth and the condition of newborns in women with HCV infection.

Materials and methods. A retrospective clinical and statistical analysis of the pregnancy course, childbirth and the condition of newborns was carried out according to the data of 351 birth histories of women with HCV infection based on the materials of the archive of the communal non-commercial enterprise “Kyiv Municipal Center of Reproductive and Perinatal Medicine” for the period from 2016 to 2021. The control group (CG) included 50 healthy pregnant women.

Results. In women with HCV infection compared to the group of healthy pregnant women a significantly high frequency (p<0.001) of such pregnancy complications was found: threat of pregnancy interruption – 64 (18.2 %) patients versus 2 (4.0 %) persons, edema of pregnant women – 72 (20.5 %) and 4 (8.0 %), respectively; preeclampsia – 45 (12.8 %) versus 2 (4.0 %), gestational anemia – 131 (37.3 %) versus 6 (12.0 %), as well as placental insufficiency with fetal growth retardation syndrome (FGR) – 69 (19.6 %) versus 3 (6.0 %); p<0.05 and intrahepatic cholestasis of pregnant women – 42 (11.9 %) versus 1 (2.0 %; p<0.05). In 73 (20.8 %) pregnant women with HCV infection the childbirth was complicated by premature rupture of the membranes, of which almost half of the cases (42 (11.9 %) of the patients) finished with premature birth, while in CG only some women had such complications. Fetal distress during childbirth was reliably detected more often in pregnant women with HCV infection than in CG women (χ²=4.76; p=0.024). Caesarean section was performed in 86 (24.5 %) patients with HCV infection versus 2 (4.0 %) persons in CG (p<0.001).

The newborns from mothers with HCV infection had lower indicators of physical development and decreased Apgar score assessment, increased frequency of conjugation jaundice.

Conclusions. Pregnant women with HCV infection are characterized by a significant increase in the number of pregnancy complications, such as the threat of pregnancy interruption, the threat of premature birth, gestational anemia, placental dysfunction, fetal growth retardation syndrome, and preeclampsia; during childbirth – premature and antepartum rupture of amniotic membranes, premature birth, weakness of uterine activity in labor, increased blood loss.

The condition of newborns from women with HCV infection is characterized by a significant increase in the frequency of asphyxia during childbirth, CNS hypoxic-ischemic damage, prematurity and conjugation jaundice.

Keywords: HCV infection, pregnancy, obstetric and perinatal complications.
Висновки. Для вагітних із HCV-інфекцією характерно достовірне збільшення кількості таких ускладнень вагітності, як загроза переривання, загроза абортів, гестозу, гестационної анемії, руйнування плаценти та поширення інфекції в пошкоджений гонадний тканин.

Ключові слова: HCV-інфекція, вагітність, акушерські та перинатальні ускладнення.

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Інаукроповідних від щонайменшого щодо HCV-інфекції характеризується достовірним підвищенням частоти афікісії під час пологів, гіпертоксично-ишемічним ураженням ЦНС, недоношеністю та кін'юкційно-жовтницею.

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Для вагітних із HCV-інфекцією характерно достовірне збільшення кількості таких ускладнень вагітності, як загроза переривання, загроза абортів, гестозу, гестационної анемії, руйнування плаценти та поширення інфекції в пошкоджений гонадний тканин.

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In Ukraine, 5% of the population is infected with hepatitis C (approximately 2 million), 3.6% have a chronic course, and only 5.4% (about 80 thousand) are under medical supervision [1–4]. The incidence of HCV infection in pregnant women reflects the prevalence of HCV infection in the relevant regions of the world. In pregnant women in the United States, as well as in Asia and Africa, the frequency of seroprevalence of the virus is 1–2.4%. This figure is higher in women who are infected with HIV. In Europe and South America – from 1% to 2%. British scientists confirm the detection rate from 0.19% to 0.43%. 60–70% of women who carry antibodies to the hepatitis C virus have an active infectious process [5–9].

Most pregnant women with HCV have a chronic lesion, and in most cases, chronic viral hepatitis occurs with minimal or weak activity. But pregnant women with acute viral hepatitis have a higher risk of morbidity and mortality compared to pregnant women with chronic viral hepatitis. The incubation period for HCV ranges from 2 to 26 weeks (an average of 6–8 weeks). Jaundice develops in 20% of sick women. Other symptoms – nausea, vomiting, pain in the right hypochondrium, darkening of the urine, are poorly expressed and characteristic of all viral hepatitis. This is why the acute phase often remains unrecognized [10–12].

Chronic hepatitis C with a minimal or weak degree of activity practically does not affect the course of pregnancy. The risk of miscarriage, complications during pregnancy and childbirth, congenital fetal abnormalities and other adverse outcomes does not exceed that of pregnant women without chronic hepatitis. However, the presence in a pregnant woman of chronic viral hepatitis of a high degree of inflammatory activity and/or cholestasis and, especially cirrhosis of the liver in the decompensation phase, as well as other aggravating factors contribute to the development of gestosis, excretory hepatitis, miscarriage and life-threatening complications during childbirth [8, 13, 14].

Some studies suggest that there is no negative effect on fetal development, but indicate intrauterine infection due to an increase in the level of viremia in the third trimester of the gestational period and an increasing risk of infection of the child during childbirth [15, 16]. Other sources in the conclusions indicate that among women with replicative forms of HCV infection, in 2.8% of cases, women with high viral load (RNA HCV – 4.65×10⁶ cop./ml), with a moderate degree of hepatitis activity, miscarriage occurred at the 18th week of gestation. The next pregnancy after 2 years, which took place on the background of therapy, with minimal cytolyis and moderate viral load in the third trimester, ended with the birth of a healthy uninfected child [17–20].

There is evidence of an adverse effect of HCV on placental structure and function. In pregnant women, in addition to the pathological process in the hepatobiary system, there are violations of placental function, in particular its pathology due to morphological and functional changes (violation of microcirculation and blood coagulation system). Due to the violation of the compensatory-adaptive mechanisms of the placenta, frequent complications of pregnancy and childbirth in HCV-infected women are early gestosis, threat of termination, intrauterine fetal hypoxia, spontaneous miscarriages at different gestation periods, premature birth, primary uterine inertia, anemia of pregnant women, developmental delay syndrome and fetal hypotrophy [1, 21].

Also, according to a study by scientists in the UK, the risk of postpartum bleeding, hepatic coma, kidney failure, coagulopathy and hepaticorenal syndrome increases for the mother. All this leads to an increase in maternal morbidity and mortality. HCV infection is closely associated with cholestasis and preterm birth. For the fetus, the incidence of abortions, preterm birth (1.6 and 3.7% of cases), and antenatal death increases, leading to an increase in miscarriages. Perinatal transmission (10–40%) is high with concomitant HIV and HCV infection, as there is a large activation of the virus against the background of immunosuppression. The risk of HCV infection in the fetus or newborn increases if the mother has drug addiction. The lowest risk of intrauterine infection occurs with HCV seroconversion during pregnancy [22, 23].

Although vertical transmission of HCV to the fetus is possible, HCV is not a contraindication to pregnancy. The level of transplacental transmission is 5–6% [10]. Infection of the child occurs mainly during childbirth, but can occur transplacentally and postnatally. The main mechanisms of infection during childbirth are considered to be the infection of maternal blood on superficial abrasions, fetal conjunctiva during passage through the birth canal, ingestion of amniotic fluid by the fetus, and so-called maternal-fetal infusions through the umbilical vein due to rupture of small placental vessels [27, 28].

Significant risk factors for perinatal HCV infection are the period of illness, the degree of mother’s viremia, the duration of pregnancy, labor management tactics, prematurity, and low body weight of the child at birth. Further research on this problem is relevant due to the need to improve the tactics of pregravidar training, prevention and treatment of obstetric and perinatal complications in women with HCV infection [27].

Thus, conducting an analysis of the course of pregnancy, childbirth and the condition of newborns in women with HCV infection will allow determining its impact on the course of pregnancy and the fetus, and developing tactics for pregnancy planning in this group of patients.

The objective: to conduct a retrospective clinical and statistical analysis of the course of pregnancy, childbirth and the condition of newborns in women with HCV infection.
MATERIALS AND METHODS

A clinical and statistical retrospective analysis of the course of pregnancy, childbirth, and the state of newborns of 351 birth histories of women with HCV infection (group I) was carried out based on the materials of the archive of KNP «Kyiv City Center for Reproductive and Perinatal Medicine» for the period 2016–2021. The control group included 50 healthy pregnant women. Statistical processing of research results was carried out using the standard programs «Microsoft Excel 5.0» and «Statistica 8.0».

Discrepancies of p<0.05 are considered statistically significant. The critical significance level when testing statistical hypotheses was assumed to be p<0.05. Comparison of nominal data was carried out by constructing compatibility tables indicating the absolute and relative (%) frequencies of occurrence of features. The Pearson χ² test was used to determine the statistical significance of the differences of the nominal features in the correlation tables, as well as the two-sided Fisher’s exact test (F), when the expected value was less than 5 [29,30].

The study was carried out in accordance with the principles of the Helsinki Declaration. The research protocol was adopted by the local ethics committee of the institution indicated in the work. Informed consent of women was obtained to conduct the study.

RESEARCH RESULTS AND THEIR DISCUSSION

Group I of pregnant women included 351 women with HCV infection who gave birth on the basis of the infectious obstetric department in the KNP «Kyiv City Center for Reproductive and Perinatal Medicine» for the period 2016–2021. The control group included 50 healthy pregnant women. The age of pregnant women with HCV infection ranged from 18 to 42 years (mean age – 27.7±0.4 years). The mean age of CG is 28.3±0.3 years. In the patient groups, the number and age of women examined were presented in different ranges (Figure).

According to the data shown in Figure, the majority of pregnant women with HCV infection and healthy ones were in the reproductive period – 263 (74.9%) and 36 (72.0%), women of the early and late reproductive period in the study groups were 88 (25.1%) and 14 (28.0%). No significant age differences were found in the compared groups (χ²=1.78, P=0.776).

Despite the rather rare clinical manifestations of HCV infection in pregnant women, pregnancy pathology was more common in them than in healthy ones. An analysis of the course of pregnancy in women with HCV infection is shown in Table 1.

Thus, compared with the group of healthy pregnant women (CG), women with HCV infection (group I) showed a significantly high frequency: threats of termination – 64 (18.2%) vs. 2 (4.0%), edema of pregnant women – 72 (20.5%) vs. 4 (8.0%), preeclampsia – 45 (12.8%) vs. 2 (4.0%), gestational anemia – 131 (37.3%) vs. 6 (12.0%).<0.001, placental insufficiency with fetal growth retardation syndrome (FGR) – 69 (19.6%) vs. 3 (6.0%) and intraperitoneal cholestasis of pregnant women (ICPW) – 42 (11.9%) vs. 1 (2.0%) p<0.05.

According to the data shown in Table 1, the course of this pregnancy in women with HCV infection in the first trimester was 1.3 times more likely than in healthy people to be complicated by early toxicosis. The threat of termination of pregnancy was more often detected in pregnant women with HCV infection compared to women of CG: 4.5 times more often. Anemia occurred in more than 1/3 of pregnant women with HCV infection, which was significantly higher than in healthy pregnant women (p<0.001). Edema of pregnant women (mainly in the third trimester) was detected in pregnant women with HCV infection 2.6 times more often than in CG women, and the incidence of preeclampsia was 3.2 times.

Intrahepatic cholestasis of pregnant women (ICPW) was diagnosed in the third trimester based on the development of severe itching of the skin, especially in the upper and lower extremities, accompanied by sleep disorders and excoriations. ICPW in healthy pregnant women occurred only in one case, while its frequency, compared with healthy women in group I, was 5.9 times higher (p=0.035).
Features of the course of labor in the examined pregnant women are shown in Table 2. The course of labor in women with HCV infection was accompanied by an increase in the frequency of premature rupture of the fetal membranes and prematurity birth.

In 7.1% of pregnant women with HCV infection, childbirth was complicated by premature rupture of the fetal membranes – 73 (20.8%) p<0.001, of which almost half of cases ended in premature birth – 42 (11.9%) cases, in CG there were isolated cases. These were mostly preterm births at 34–36 weeks. Early outpouring of amniotic fluid – 12 (3.4%) vs. 1 (2.0%) in CG and abnormal labor (mainly in the form of primary weakness) – 38 (10.8%) vs. 4 (8.0%) p>0.05, were equally common in the study groups.

Preterm birth (up to 37 weeks) ended in 42 (11.9%) women with HCV infection, while healthy pregnant women gave birth between 38 and 40 weeks. In one case, in a pregnant woman with HCV infection, preterm labor at 34 weeks of gestation resulted in intranatal fetal death as a result of tight cord entanglement. According to Table 2, fetal distress during childbirth was significantly more common in pregnant women with HCV infection than in CG women (χ2=4.76; p=0.024). Caesarean section in СG there were isolated cases. These were mostly preterm births at 34–36 weeks. Early outpouring of amniotic fluid – 73 (20.8%) p<0.05, were equally common in the study groups.

Blood loss of up to 250 ml accompanied significantly more frequent labor in CG (81±3.9%) compared to 50±7.1% of labor in women with HCV infection (p<0.05). Blood loss from 251 to 500 ml was recorded more often in women of group I 55±11.1% (p=0.001) vs. 7.0±2.6% in CG. The percentage of blood loss with a volume of 501 to 1000 ml was as follows – in CG (12±3.5%) at 5.4±9.7% in group I (p>0.05). The average blood loss in CG was 237±11.5 ml at 283±9.2 ml in group I of women (p<0.05).

Physical health parameters of newborns from mothers with chronic hepatitis С were evaluated based on physical parameters and Apgar scores at birth (Table 3). The average scores on the Apgar scale at 1 minute of life are higher in CG newborns – 7.57±0.84 in the group I (p<0.05), and already at 5 minute these indicators were equal to 8.54±0.67 in CG at 7.48±0.67) in the group I (p>0.05).

The data presented in Table 3 show lower body weight and length values in newborns from women with HCV infection compared to children from healthy women (p<0.05). In addition, the Apgar score at birth (p<0.001) was lower in children from mothers with HCV infection. An Apgar score below 7 points was diagnosed in 7.4% (26/350) of children from mothers with HCV infection (F=4.61, p=0.032), which was significantly higher than in newborns from healthy mothers.

Frequency of conjugation jaundice in newborns from healthy mothers (Table 4) was 4.0% (2/50), while in children from mothers with HCV infection – 10.3% (36/350) (χ2=7.97; p=0.005). Correlation analysis conducted in children from mothers with HCV infection found that the Apgar score has positive associations of average strength with body length (τ=0.266; p<0.001), and the development of conjugation jaundice in newborns has average negative correlations with physical parameters at birth such as body weight (τ=-0.302; p<0.001) and body length (τ=-0.306; p<0.001), as well as with the Apgar score (τ=-0.302; p<0.001) and gestational age at birth (τ=-0.249; p<0.001).

When analyzing the number of mild and moderate asphyxia, their significant (p<0.05) growth was found in newborns, from mothers with HCV infection – 79 (22.4%) cases vs. 2 (4.0%). In turn, severe asphyxia was established only in newborns from women with HCV infection – 9 (2.6%) cases. Newborns from women with HCV infection were significantly more likely to suffer from acute ischemic lesions of the central nervous system.
(p<0.001) – 58 (16.6%) vs. 3 (6.0%) cases per CG. FGR syndrome was significantly (p<0.05) more common in newborns from women with HCV infection – 61 (17.3%) cases vs. 2 (4.0%) cases in CG newborns.

The condition of newborns from mothers with HCV infection was significantly (p<0.05) more common in cases vs. 2 (4.0%) cases in CG newborns. An assessment of the influence of the pathological course of pregnancy and childbirth on the clinical parameters of newborns is given in Table 5.

As shown in Table 5, a decrease in the Apgar score at birth had a significant association with premature rupture of the fetal membranes, as well as a very pronounced association with preterm birth. The development of conjugation jaundice in newborns was significantly associated with the presence of anemia and the threat of termination in the mother, as well as a very strong association with premature rupture of the fetal membranes and premature birth.

Thus, newborns from mothers with HCV infection had lower physical development parameters and a lower Apgar score, as well as an increased incidence of conjugation jaundice. The physical and clinical parameters of newborns from mothers with HCV infection were associated with pathological conditions during pregnancy.

Data from modern foreign and domestic literature are very contradictory about the influence of HVC on the course of pregnancy, childbirth and the condition of newborns [5, 8, 9, 12, 13, 14, 19]. So, many researchers claim that chronic hepatitis C with a minimal or weak degree of activity practically does not affect the course of pregnancy. The risk of miscarriage, complications during pregnancy and childbirth, congenital fetal abnormalities and other adverse outcomes does not exceed that of pregnant women without chronic hepatitis. However, the presence in a pregnant woman of chronic viral hepatitis of a high degree of inflammatory activity and/or cholestasis and, especially cirrhosis of the liver in the decompensation phase, as well as other aggravating factors contribute to the development of gestosis, excretory hepatosis, miscarriage and life-threatening complications during childbirth [8, 13, 14].

And some authors confirm the adverse effect of viral hepatitis C on the structure and function of the placenta. In pregnant women, in addition to the pathological process in the hepatobiliary system, there are violations of placental function, in particular its pathology due to morphological and functional changes (violation of microcirculation and blood coagulation system). Due to the violation of the compensatory and adaptive mechanisms of the placenta, frequent complications of pregnancy and childbirth in HCV-infected women are early gestosis, the threat of termination, fetal distress, the threat of spontaneous miscarriages at different gestation periods, premature birth, primary uterine inertia, gestational anemia, fetal growth retardation syndrome [1, 21]. These data coincide with those obtained by us when analyzing the course of pregnancy, childbirth, and the condition of newborns in women with HCV infection and indicate a significant increase in pregnancy and childbirth complications in this group of women.

### Table 5

<table>
<thead>
<tr>
<th>Complications</th>
<th>Reduced Apgar score at birth OSH (95% CI), p</th>
<th>Development of conjugated jaundice OSH (95% CI), p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICPW</td>
<td>0.42 (0.14-2.68), p=0.516</td>
<td>1.65 (0.79-3.43), p=0.180</td>
</tr>
<tr>
<td>Early toxicosis</td>
<td>0.89 (0.21-3.98), p=0.891</td>
<td>1.96 (0.87-4.45), p=0.101</td>
</tr>
<tr>
<td>Gestational anemia</td>
<td>1.19 (0.55-2.56), p=0.656</td>
<td>1.92 (1.17-3.19), p=0.01</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>1.06 (0.23-2.73), p=0.716</td>
<td>1.28 (0.64-2.57), p=0.488</td>
</tr>
<tr>
<td>Threat of termination</td>
<td>1.45 (0.94-2.66), p=0.081</td>
<td>1.89 (1.04-3.42), p=0.034</td>
</tr>
<tr>
<td>Placental insufficiency with FGR syndrome</td>
<td>1.38 (0.57-3.33), p=0.471</td>
<td>1.09 (0.58-2.04), p=0.786</td>
</tr>
<tr>
<td>Complications in childbirth</td>
<td>0.79 (0.23-2.73), p=0.720</td>
<td>1.79 (0.92-3.50), p=0.085</td>
</tr>
<tr>
<td>PPROM</td>
<td>3.35 (1.27-8.87), p=0.001</td>
<td>8.32 (3.89-17.58), p&lt;0.001</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>7.62 (3.23-17.98), p&lt;0.001</td>
<td>29.06 (11.41-74.03), p&lt;0.001</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>0.80 (0.29-2.17), p=0.657</td>
<td>0.70 (0.36-1.34), p=0.275</td>
</tr>
</tbody>
</table>

### CONCLUSIONS

For pregnant women with HCV infection a significant increase in such complications is characteristic – during pregnancy: the threat of termination, the threat of premature birth, gestational anemia, placental dysfunction, fetal growth retardation syndrome, preeclampsia; – during childbirth: premature and prenatal outpouring of amniotic fluid, premature birth, poor uterine contraction strength, increased blood loss.

The condition of newborns from women with HCV infection is characterized by a significant increase in the frequency of asphyxia during childbirth, hypoxic-ischemic damage to the central nervous system, prematurity and conjugation jaundice.

The authors state that there is no conflict of interest.
REFERENCES


