



PREGNANCY IN HCV POSITIVE PATIENTS

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ABSTRACT

The HCV prevalence in the European Union and Economic Area countries is approximately 1.1% in total, which accounts for 5.6 million anti-HCV positive and 3.9 chronically infected individuals. According to the Polish regulations, every pregnant woman should be screened for HCV until the 10th gestational week. Repeat HCV screening is recommended between 33rd-37th week of gestation among women from high-risk groups. Large population-based studies have proved higher incidence of certain adverse pregnancy outcomes, including gestational diabetes, preterm delivery, low birth weight, small for gestational age, and intrahepatic cholestasis of pregnancy in pregnancies complicated with chronic maternal HCV infection. In addition, one of possible complications is mother to child transmission. There is no evidence to support the use of elective caesarean section and recommend it as transmission prevention. Risk factors which should be prevented in order to decrease the transmission rate include: detectable viremia, especially exceeding 107 IU/ml, exposure to maternal blood, rupture of membranes and amniotic fluid leakage lasting over 6 hours, invasive prenatal diagnostic procedures, and maternal coinfection with HIV. Appropriate screening and viremia control seem to be most relevant in the antenatal management of HCV positive women.

BACKGROUND

Hepatitis C is a major problem among pregnant women. It has been estimated that up to 29,000 HCV-infected women gave birth each year from 2011 to 2014 [1]. Following article describes problems which obstetrician should take care of during high-HCV risk pregnancy.

PREVALENCE

In 70-90% of cases the initial infection with hepatitis C virus (HCV) is asymptomatic, but as many as 70-80% of HCV positive patients will develop chronic infection leading to hepatic cirrhosis after 20-30 years in every fifth untreated individual and hepatocellular cancer (HCC) in 1-5% of the infected population [1]. Up to 90% of those infected remain unaware of their condition and cannot be efficiently managed prior to development of long-term health consequences, which is why it is estimated that despite the availability of effective treatment options, the burden of HCV-caused mortality will continue to rise as the population ages [2, 3, 4]. Transmission of HCV can occur during sexual contact, blood-to-blood contact, and vertically – from the mother to the child during the antenatal and perinatal period [5]. It is estimated that globally 184 million people are infected with HCV [6]. The number of deaths caused by HCV-induced liver disease is 350 000-500 000 every year [7].

The HCV prevalence in the European Union (EU) and Economic Area (EEA) countries is approximately 1.1% in total, which accounts for 5.6 million anti-HCV positive and 3.9 chronically infected individuals [8]. Anti-HCV prevalence in pregnant women is considerably lower than in the general population ranging from 0.1% to 0.9% depending on the region [8]. These differences are caused by the fact that 60% of HCV infections concern patients over 65 years of age as well as high risk groups in Europe include men who have sex with men (MSM), people who inject drugs (PWID) and people in prison [9]. Management of sexually transmitted infections (STIs) among pregnant women together with screening and prevention of vertical transmissions might be an even greater challenge in the low and middle income countries. According to the study by Benhammou et al, prevalence of anti-HCV among pregnant women in the Southwestern Nigeria was 2.7%, which is 3-27 times higher than in the EU/EEA cohort [10]. Even more alarming are the results of screening of pregnant women attending antenatal care in the Western Ethiopia as HCV seroprevalence in this population was as high as 8.1% [11].

SCREENING

Screening performed among the group of pregnant women is not only relevant due to prevention of vertical transmission, but also gives opportunity of eradication of the detected virus in infected women postpartum. However, it is not routinely performed as part of standard antenatal care not only in the developing countries, but also in the United States. Clinical guidelines concerning HCV screening vary. The Society of Maternal-Fetal Medicine (SMFM) and American College of Obstetrics and Gynecology (ACOG) both recommend HCV screening limited to pregnant women from high risk

groups [12, 13]. The U.S. Center for Disease Control (CDC) recommends routine antenatal screening for HIV, hepatitis B virus, and syphilis, but not for HCV [14]. On the other hand, the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (AASLD-IDSA) recommends routine HCV screening in every pregnant woman, ideally in the beginning of prenatal care [15].

According to the Polish regulations, every pregnant woman should be screened for HCV until 10th gestational week. Repeat HCV screening is recommended between 33rd-37th week of gestation among women from high-risk groups [16]. Routine HCV screening as part of standard prenatal care in Poland was first introduced in 2010, leading to higher detection of HCV infection in women not presenting any risk factors (9.9% before 2010 vs 46.1% after 2010) [17].

According to the study by Chaillon et al., universal prenatal HCV screening is not only clinically relevant, but also cost-effective, being beneficial even in case of the lowest prevalence state in the United States (Hawaii, HCV prevalence 0.07%). With the estimated average prevalence of HCV chronic infections among pregnant women equal to 0.73%, detection and treatment in case of universal screening would allow helping 33 000 women in the US yearly [18].

ACUTE HCV INFECTION IN PREGNANCY

In non-pregnant population, most acute HCV infections are asymptomatic or cause non-specific symptoms including loss of appetite and malaise. Acute hepatitis accompanied by icterus is present in 10-20% of patients. In about 20–25% of acute infections viremia spontaneously resolves due to immune reactions. However, in the majority of cases, acute hepatitis is followed by chronic, lifelong infection. The chronic phase is characterized by stable high-level viremia and normal or elevated transaminase enzymes. Affected individuals are usually asymptomatic [19, 20].

The exact impact of pregnancy on the outcome of acute HCV infection is unknown, but it is suspected that the immunomodulation could predispose to development of chronic infections [21]. At the same time it is unknown if acute infection during pregnancy is more likely to result in mother to child transmission (MTCT) or adverse pregnancy outcomes than chronic infection. Reports of premature delivery in patients with acute HCV infection in the third trimester are available in literature [21, 22].

PREGNANCY COMPLICATIONS

Several studies have indicated association between chronic HCV infections and increased risk of caesarean section [23, 24, 25]. Large population-based studies have proved higher incidence of certain adverse pregnancy outcomes, including gestational diabetes, preterm delivery, low birth weight, small for gestational age, and intrahepatic cholestasis of pregnancy in pregnancies complicated with chronic HCV infection [26, 27, 28, 29, 30, 31].

One of possible complications of maternal HCV infection in pregnancy is MTCT. There are several routes

suspected to be responsible for intrauterine HCV transmission: transcytosis, trafficking in maternal mononuclear cells, receptor mediated entry, trophoblast infection, and injury of the placental barrier [32, 33, 34, 35]. The first factor associated with increased risk of MTCT is viremia exceeding 107IU/ml, whereas undetectable viral loads are concerned as safe [36, 37, 38, 39]. Other identified MTCT risk factors include exposure to maternal blood, rupture of membranes and amniotic fluid leakage lasting over 6 hours, invasive prenatal diagnostic procedures, and maternal coinfection with HIV [36, 40, 41].

DELIVERY

There is not enough evidence to support the use of elective caesarean section in MTCT prevention. The Cochrane Review on this topic states: "Currently there is no evidence from randomised controlled trials upon which to base any practice recommendations regarding planned caesarean section versus vaginal delivery for preventing mother to infant Hepatitis C Virus transmission" [42].

Huge discussion concerning effectiveness of elective caesarean sections in MTCT prevention was initiated by Gibb et al. results. In this multicentre prospective cohort study authors observed the following transmission rates depending on the delivery method: 7.7% for vaginal birth (339 patients), 5.9% for emergency caesarean section (54 patients), 0% for elective caesarean section (31 patients) [43]. However, many authors reported no association between the method of delivery and decreased MTCT rates [44, 45, 46].

CONCLUSIONS

Two main conclusions arise from the presented literature review. The first one concerns the relevance of screening and detection of otherwise asymptomatic patients with HCV infection, who can receive proper treatment and avoid development of grave hepatic consequences. The other one relates to appropriate control of viremia in pregnancy being the most important factor decreasing risk of vertical transmission and refuting the myth of elective caesarean sections as a miracle cure for MTCT.

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ABBREVIATIONS

AASLD-IDSA – the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America
ACOG – American College of Obstetrics and Gynecology
CDC – Center for Disease Control
EU/EEA – the European Union and Economic Area countries
HCC – hepatocellular cancer
HCV – hepatitis C virus
MTCT – mother to child transmission
MSM – men who have sex with men

PWID – people who inject drugs

SMFM – Society of Maternal-Fetal Medicine

STIs – sexually transmitted infections

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