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REVIEW ON: ANALYSIS AND CONTROLLING OF HEPATITIS C VIRUS IN INFECTED PREGNANT WOMEN AND THEIR DIAGNOSIS

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ABSTRACTS

Hepatitis C is, at present, a worldwide health problem and is the most common cause of liver transplantation. Its prevalence in pregnant women is similar to that of the general population. In the absence of cirrhosis and portal hypertension, most HCV-infected pregnant women do not have obstetric complications. Screening of pregnant women that are asymptomatic and do not have risk factors is not cost effective. A high hepatitis C viral load reportedly increases vertical transmission and is higher in women who are co infected with HIV or who are intravenous drug users. Prolonged rupture of the membrane for more than 6 h, amniocentesis, and perineal lacerations increase the potential risk of perinatal transmission. Although the hepatitis C virus can be transmitted intrapartum, prevention by caesarean delivery is not generally indicated. The HCV virus can be found in maternal milk; however, breast feeding is not contraindicated. In conclusion, there are no antiviral treatment recommendations for HCV-infected women during pregnancy, or guidelines for the prevention of vertical transmission.

KEYWORDS: Vertical Transmission, Intrapartum, Hypertension, Perineal Lacerations Etc.

INTRODUCTION

Hepatitis C virus (HCV) infection remains a leading reason of liver disease worldwide. The goal of World Health Organization is to significantly reduce the rates of mortality and morbidity due to HCV by 2030. To achieve this goal a tremendous effort is required for identification and treatment of HCV positive individuals.[1,2] Hepatitis C infection is instigated by the hepatitis C virus (HCV). The symptoms of HCV infection include nausea and jaundice, but most cases it is asymptomatic. Occasionally, the HCV is self-cleared by the body, but usually the HCV lives in the liver for long.[3] This virus might stay alive

for years without causing any major health concerns, however, some can cause liver cirrhosis and liver cancer. These problems generally occur after several years of getting exposed to HCV. Apart from the advancement in pathogenesis and treatment of Hepatitis C, HCV infection in pregnant women has been an ignored condition. Pregnant women with HCV infections have a 2-8% risk of mother to child transmission (MTCT).[4] But, usually the history of the disease in pregnant females and their offspring is often ignored. Therefore, identification of pregnant women with HCV-infection is relevant as the infection may result in long-lasting health issues for the mother, ill effects of infection on pregnancy outcomes, and risk of MTCT.[5] HCV is primarily transmitted through percutaneous contact to blood from injection of illicit drugs. Other means of HCV transmission include MTCT, using contaminated devices for drug delivery, introduction of contaminated blood, and by sexual intercourse up to a lesser extent. The impact of HCV infection on pregnancy and perinatal consequences is the main issue resulting from HCV infections in pregnancy, and this concern must be addressed wisely for wellbeing of mother and the offspring.[6,7]

Impact of Hcv Infection on Pregnancy And Perinatal Consequences

HCV infection during pregnancy has shown to increase risk of adverse perinatal consequences including premature delivery, infants with low birth weight, and inborn defects. Yet, the pregnant women with cirrhosis might witness more complications and problems such as caesarean section, preeclampsia, haemorrhagic issues, and death, in addition to neonatal consequences such as premature delivery, low birth weight of new-born, and death of neonate.[8,9]

The prevalence of MTCT of HCV infection is 5% to 15%, of which 3% to 5% witness chronic infection. Neither a definite risk factor envisages transmission nor has any definite involvement (such as antiviral therapy or mode of drug) been established to reduce transmission of HCV. However, the risk of MTCT, can be reduced by avoiding invasive procedures such as forcep delivery.[2]

Screening/ Diagnostic Tests For Hcv

HCV infection is diagnosed by two methods i.e. screening of anti- HCV antibodies and HCV RNA. In acute phase of infection, anti-HCV antibodies are generally produced after 2-6 months of exposure and one can survive throughout the life. HCV viremia indicates the occurrence of HCV RNA in sample of blood, and causes active infection, which can be

detected within 1-3 weeks after exposure.[10] An anti-HCV antibody assay is one of the standard screening test method for HCV detection. Positive result for the test shows that the patient has one of the following; an active infection that may be acute or chronic, patient is either recovered from prior infection, or outcome is false positive. Positive result for anti-HCV antibody must be confirmed from quantitative assay of HCV RNA.[11] If a patient without a previous hepatitis C examination has tested positive for anti-HCV antibodies as well as HCV RNA, then it is impossible to differentiate acute and chronic HCV infection on the basis of test results. When the outcome of the anti-HCV antibody test is found positive and the result of the HCV RNA test is found negative, it is not possible to differentiate between a false-positive antibody test and a true infection and to differentiate between these two a comparison test for anti-HCV antibody and another different antibody is required. Further, if a patient who was exposed to HCV has been adversely screened for anti-HCV antibodies and found negative, during the last 6 months, HCV RNA monitoring should be undertaken as the patient could still not have been seroconverted.[12,2] Various diagnostic tests for HCV infection have been presented in Figure 1.

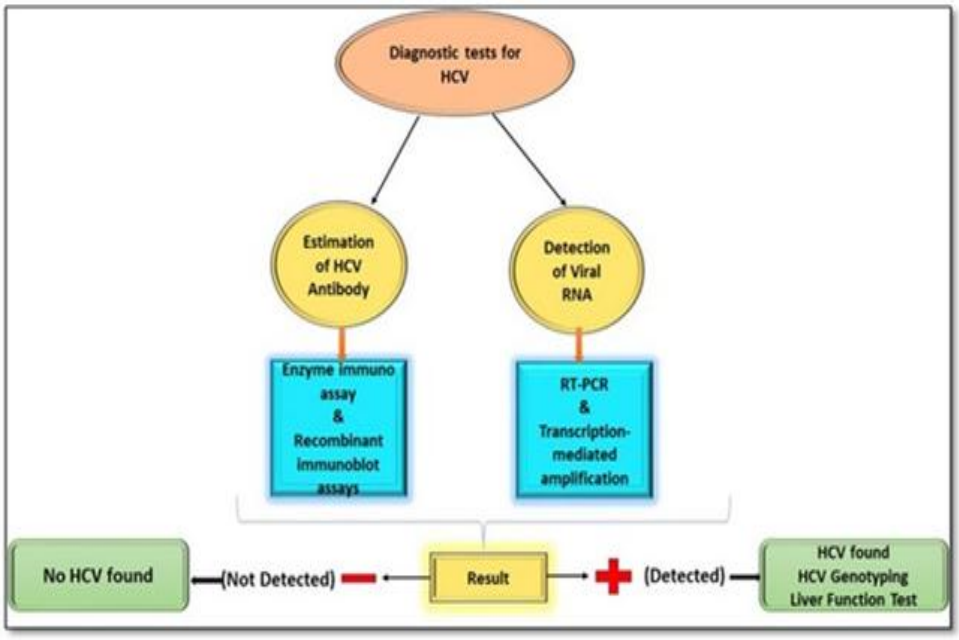

Figure 1: Various diagnostic tests for HCV infection.

Treatment of Hcv During Pregnancy

Combination therapy with ribavirin and pegylated IFN-α for a period of 24- 48 weeks is considered as standard therapeutic option for infection with HCV. However, due to

safety issues this treatment option in pregnancy is not recommended. Particularly, Ribavirin is contraindicated in pregnancy as at low doses, the drug has been shown to produce teratogenic outcome in numerous in-vivo animal studies, but teratogenic effect in humans has not been established yet. Ribavirin owns a long half-life, and its 6 months prior avoidance is suggested for the couples planning to conceive.[13] Direct-acting antivirals (DAAs) are the key therapeutic options for the management of HCV infection during pregnancy as well as post-delivery care of new-borns infected with HCV.

The obtainability of highly effective DAAs and the option of using them during pregnancy hasbeen initiated to be explored.[14] Various DAAs have now been categorised as pregnancy category B, confirming that the DAAs are safe and non-toxic to the foetus as proved in animal studies in-vivo, however adequate human trials are still to be explored. Phase 1 trial assessing ledipasvir/sofosbuvir during the lats months of pregnancy is under way, and results are expected soon. Another research for assessing the usage of sofosbuvir/ velpatasvir after delivery (after breastfeeding) is accomplished. Investigators all over the world have already begun to establish protocols for the treatment of HCV treatment during pregnancy. Till today no findings of adverse pregnancy outcomes has been reported for sofosbuvir/ velpatasvir.[15,16] One more drug molecule i.e. pegylated IFN-α belonging to pregnancy category C of FDA, is used for HCV infection during pregnancy, but its involvement in pregnancy is limited, though a recent finding on IFN-α suggested no adverse fatal outcomes during pregnancy. Treatment with IFN-α in the post-delivery period is not recommended for breastfeeding mother, and also for the non-breast-feeding mother owing to its significant side effects. Nevertheless, innovations in HCV drug development have preserved a constant hope for HCV therapy and a decade ago, telaprevir and boceprevir (protease inhibitors) were approved FDAfor HCV genotype 1 infection.[2]

Recommendations For Monitoring Hcv-Infected Women During Pregnancy

- HCV-antibody–positive pregnant women should be recommended for routine liver function tests (LFT) and HCV RNA test to assess the risk of MTCT and disease severity.
- All the HCV positive pregnant women should get suitable prenatal and intrapartum care to avoid their individual obstetric risk(s) as there is no appropriate treatment is available to reduce MTCT.[17]

- HCV-positive pregnant women with cirrhosis should be made aware about the enhancedrisk of perinatal and maternal adverse outcomes.[10]
- HCV-positive pregnant women having jaundice/ pruritus, must be assessed for alanine aminotransferase, aspartate aminotransferase, and serum bile acids to examineintrahepatic cholestasis

Recommendations for Breastfeeding and Post-delivery Care for HCV-infected women Breastfeeding is contraindicated in women with HCV infection, if the mother is HIV positive or ifshe is having injured, or haemorrhagic nipples.[17]

CONCLUSION

The occurrence of HCV among pregnant women is increasing worldwide, and recent recommendations by WHO are to screen all the pregnant women for HCV, irrespective of risk associated with the infection. But majority of the pregnant women infected with HCV are still unidentified, therefore optimal management of HCV-positive pregnancies has not developed yet. For efficient treatment of HCV, risks and benefits to the women and her offspring must be examined. More safety data on usage of antivirals during pregnancy is instantaneously needed and in upcoming time the treatment protocol for these drugs in pregnancy would be available soon after the clinical trials findings on usage of DAAs are available. Besides this, better understanding about HCV-specific immunity both before and after the pregnancy can guide latest approaches for treatment. When effective approaches for prevention of MTCT are established, or suitable pharmacotherapies are found for this, in pregnancy, arguments against extensive HCV screening can be nullified.

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