



Symposium on liver & pregnancy

Effect of pregnancy on pre-existing liver disease: Chronic viral hepatitis

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Abstract

Women with viral chronic hepatitis generally do quite well during pregnancy, providing that they have not progressed to decompensated cirrhosis. As a general rule, a stable liver equals a safe pregnancy. However, concern is about how pre-existing chronic liver disease may affect the pregnancy and the unborn baby. This review plans to answer some key questions regarding this issue in order to provide to healthcare professionals updated information of the current knowledge in this field. Besides, a synopsis of the following subject matters are reviewed, for instance, the main risk factors associated with vertical transmission of HBV and HCV in pregnant women chronically infected, the influence of pregnancy on HBV and HCV viral load and the effect of pregnancy on the clinical course of chronic hepatitis. Lastly, it is included a list of recommendations to decrease vertical transmission rates of chronic viral hepatitis as well as some information for the reproduction team.

Key words: Pregnancy, viral hepatitis, hepatitis B, hepatitis C, chronic liver disease.

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List of abbreviations:

Hepatitis B virus, HBV.
Hepatitis C virus, HCV.
Human immunodeficiency virus, HIV.
Peripheral blood mononuclear cells, PBMCs.
ALT, alanine aminotransferase.
Hepatitis B Immunoglobulin, HBIG.

Women with viral chronic hepatitis generally do quite well during pregnancy, providing that they have not progressed to decompensated cirrhosis. As a general rule, a stable liver equals a safe pregnancy.

However, concern is about how pre-existing chronic liver disease may affect the pregnancy and the unborn baby. This review plans to answer some key questions regarding this issue in order to provide to healthcare professionals updated information of the current knowledge in this field.

Vertical transmission of hepatitis B and C in pregnant women with chronic hepatitis

Vertical transmission of hepatitis B virus (HBV) is the main cause of chronic HBV infection in endemic areas. When the mother is a chronic HBsAg carrier (and positive for viral DNA in her serum), the risk of the neonates to become a chronic carrier himself is closed to 80 to 90%.¹

In the opposite, if the mother is negative for viral DNA in the serum, the transmission rate is about 10 to 30%.²

In the case of hepatitis C virus (HCV), the risk of perinatal transmission is approximately 4% to 10%, although reported rates of transmission vary depending on virus genotype, co-infection with human immunodeficiency virus (HIV) and titer of HCV-RNA in the mother.^{3,4} Risk is more important if the woman had elevated levels of viral load ($> 10^5$ copies/mL) and if the duration between membrane rupture and delivery is long.³ Overall, risk of perinatal transmission of HCV appears extremely low if mother is HCV-antibody positive but HCV-RNA negative at the time of delivery. Besides, risk is less than 10% in HIV negative mothers, compared with at least 50% HIV-co-infected mothers.⁵

When does mother-to-child transmission of hepatitis virus occur?

There are three possible routes of transmission of hepatitis virus from infected mothers to infants: transplacental transmission in uterus (antenatal transmission), transmission during delivery and postnatal transmission from mothers to infants during child-care or through breast-feeding.⁶

The baby usually first encounters the virus upon entering the birth canal, particularly in HCV infection. Virus in

the blood and vaginal fluids of the mother readily expose the baby to the disease during delivery.^{7,8} Nonetheless, it was reported that at least one third and up to a half of infected children acquired infection in uterus.^{9,10}

Conversely, in the case of HBV infection, several evidences demonstrate that in uterus infection plays an important role.¹¹ Besides, most researchers hold that the mechanism of HBV intrauterine infection is transplacental infection. In fact, it was suggested that transplacental leakage of HBeAg-positive maternal blood, which is induced by uterine contractions during pregnancy and the disruption of placental barriers, is the most likely route to cause HBV intrauterine infection.¹²

In addition, it was shown that the main risk factors for intrauterine HBV infection are maternal serum HBeAg positivity, history of threatened preterm labor, and HBV in the placenta especially the villous capillary endothelial cells.¹³

Therefore, the presence of HBsAg in cord blood may indicate intrauterine infection. Unfortunately, intrauterine transmission of HBV can be a possible cause of vaccination failure and spread of HBV.

An interesting finding is the fact that some of the fetuses that have contact with HBV antigens early in embryonic development may become immunologically tolerant to HBV antigens.¹⁴

Finally, in both HBV and HCV chronic infection, high maternal viremia and intrapartum exposure to virus-contaminated maternal blood increased the risk of virus transmission during vaginal deliveries.

Which are the main risk factors associated with vertical transmission of HBV and HCV in pregnant women chronically infected?

The main risk factor for vertical transmission of HBV seems to be mother viral load. Accordingly, maternal HBV-DNA seems to be a stronger independent predictor of persistent infection than HBeAg status. In effect, vertical transmission was most frequently seen in HBeAg-positive mothers with very high levels of viremia.¹⁵

Additionally, it was reported that among HBeAg-negative mothers, the Odds Ratio for having a persistently infected infant was 19.2 (95% confidence interval, 2.3-176.6) in mothers with high versus low levels of serum HBV-DNA.¹⁶ Thus, perinatal exposure to high levels of maternal HBV-DNA is the most important determinant of infection outcome in the infant.

On the other hand, it was suggested that the outcome of HBV infection in newborns depends not only on the host's immunocompetence and on viremia level in maternal blood, but also on heterogeneity of HBV. Transmission of mixed HBV populations appears associated with an early immunoelimination of the virus, while infection with wild-type HBV alone contributes to induction of chronicity.¹⁷ Specific allelic mutations in maternal HBV

and level of maternal viremia are potential predictors of vertical breakthrough infection.¹⁸

In the case of HCV, again one of the most important risk factor associated with vertical transmission is the level of viral load.¹⁰

In a large prospective study evaluating the risk of vertical HCV transmission, 75,909 pregnant women were tested for anti-HCV, and 567 (0.75%) were confirmed as being HCV positive.¹⁹ Interestingly, among HIV-negative mothers, geometric mean HCV-RNA levels were higher in those who transmitted HCV (8.9×10^6 genome copies/mL) than in those who did not transmit HCV (2.2×10^6 genome copies/mL).¹⁹

Viral heterogeneity of HCV also represents an additional risk factor for vertical transmission. Despite few studies have focused on the role of HCV genotypes as a risk factor, HCV genotypes 1b and 3a seem to be the most commonly transmitted in one report²⁰ while in other study, infants infected with genotype 1 were significantly more likely to have evidence of intrauterine infection than those with other genotypes.⁹

Strongly related with the mentioned factors are the fact that infection of peripheral blood mononuclear cells (PBMCs) with HCV has been demonstrated and has been found to play a role in relapse of HCV disease and vertical transmission of HCV.²¹ However, the mechanism through which HCV infection of PBMCs favors vertical transmission of the virus is still incompletely understood.

HCV infection is common in HIV infected individuals. Maternal co-infection with HIV type 1 as previously described, is a factor consistently associated with an increased risk of perinatal HCV transmission,⁷ may be related to higher viral replication in HCV-HIV co-infected patients.

Between the maternal risk factors that may increase perinatal transmission it is worth to mention the history of drug use, independently of HIV infection.²² It may be explained given that drug use is thought to impair function of the immune system and to induce tolerance to viral infections.

Another remarkable risk factor is the relationship between HCV-related disease activity in the mother and the likelihood of HCV transmission to their infants. In a recent study that evaluated seventy-four transmitting and 403 non-transmitting mothers, abnormal ALT levels were found more frequently in HCV transmitting ones, showing that the risk of transmission from mothers with constantly raised ALT levels was more evident than that from mothers with fluctuating or normal ALT levels.²³

Lastly, some obstetrical factors may be related with higher risk of vertical HCV transmission. For instance, among infants born to HCV infected-HIV negative mothers, longer duration of membrane rupture and invasive fetal monitoring were associated with transmission.²⁴ In the same way, in the study of Mast et al. previously mentioned, in multivariate analysis restricted to HCV-RNA

positive mothers, membrane rupture $> \text{ or } = 6$ hours (odds ratio, 9.3 [95% CI, 1.5-179.7]) and internal fetal monitoring (odds ratio, 6.7 [95% CI, 1.1-35.9]) were associated with transmission of HCV to infants.¹⁹

In *Table I and Table II* are summarized the risk factors for vertical transmission of HBV and HCV.

How does pregnancy influence HBV and HCV viral load in women with chronic hepatitis?

Information is paucity about how pregnancy influences viremia levels in women with chronic hepatitis B virus infection.

In a retrospectively study that analyzed the changes in HBV-DNA levels during and after 55 pregnancies in HBsAg positive women, it was shown that although the majority of HBeAg negative women had low and relatively stable HBV-DNA during pregnancy, viremia was also relatively high in some HBeAg negative mothers, and both viremia and ALT increased significantly late in pregnancy or shortly after delivery (15). The authors also found that HBV-DNA increased by a mean of 0.4 log late in pregnancy or early post partum and that HBV-DNA ranged from 10^{10} copies/mL in HBeAg positive, and from undetectable (< 100 copies/mL) in HBeAg negative mothers.

Regarding HCV infection, several studies showed that in pregnant women with chronic hepatitis C, serum HCV-RNA levels increase during the second and third trimesters²⁵⁻²⁷ suggesting the importance of immune mediated mechanisms in controlling the viral replication.

On the contrary, Hattori et al. reported that significantly more pregnant women lost the HCV-RNA than did non-pregnant controls suggesting that pregnancy and parturition appear to influence the clinical course of HCV infection.²⁸

How does pregnancy influence the clinical course of chronic hepatitis?: Liver function tests in pregnant women with chronic hepatitis.

In the case of chronic HCV infection, unlike viral load -that may increase late in pregnancy-, transaminases tend to normalize from the baseline levels during the second and third trimesters of pregnancy.²⁵⁻²⁷ This observation may support the hypothesis of a favorable and perhaps immune-mediated effect of pregnancy on liver cell necrosis in anti-HCV positive women.²⁹ Hence, the pregnancy does not induce a deterioration of liver function.

Concerning to chronic HBV infection during pregnancy, it was shown that both viral load and ALT increase significantly late in pregnancy or shortly after delivery.¹⁵ However, it is important to note that ALT levels have low sensitivity as surrogate marker for high HBV-DNA level, since it was reported that no correlation between ALT and HBV-DNA levels was found.³⁰

Lastly, it is worthy of note that all markers of liver function are generally reduced or low during pregnancy

Table I. Risk factors associated with vertical transmission of HBV in pregnant women chronically infected.

| |
|---|
| <ul style="list-style-type: none"> • Viral factors High levels of HBV-DNA Presence of HBV in the villous capillary endothelial cells Infection with wild-type HBV alone Specific allelic mutations in maternal HBV • Obstetric factors Long duration of membrane rupture History of threatened preterm labor Transplacental leakage of HBeAg-positive maternal blood |
|---|

Table II. Risk factors associated with vertical transmission of HCV in pregnant women chronically infected.

| |
|---|
| <ul style="list-style-type: none"> • Viral factors High levels of HCV-RNA viral load Infection with genotype 1b and 3a Presence of HCV-RNA in PBMCs Co-infection with HIV-1 • Obstetric factors Long duration of membrane rupture History of threatened preterm labor Invasive fetal monitoring • Maternal factors History of drug use Disease activity (persistently elevated ALT levels) |
|---|

due to the expansion of extracellular fluid. Hence serum albumin, transaminases (AST and ALT) and total bilirubin are low compared with the non-pregnant state. The only exception is serum alkaline phosphatase that is elevated due to ALP of placental origin.

Should be offered an elective cesarean to pregnant women with chronic hepatitis?

Although cesarean delivery has been proposed as a means of reducing mother to child transmission of HBV,³¹ the mode of delivery does not appear to have a significant effect on the interruption of HBV maternal-baby transmission.³² In effect, is not presently recommended by either the CDC (Centers for Disease Control)³³ or the American Academy of Pediatrics or the American College of Obstetricians and Gynecologists^{32,34} delivery by cesarean for the purpose of reducing vertical transmission of HBV. Regarding HCV, the European multi-center prospective study of HCV-infected pregnant women and their infants showed that there was no protective effect of elective cesarean delivery on HCV vertical transmission (adjusted odds ratio, 1.46 [95% CI, 0.86-2.48], $P = 0.16$) in comparison with vaginal delivery.³⁵

On the contrary, other authors that examined the effect of mode of delivery on vertical HCV transmission observed significantly lower transmission rates with cesarean section, showing that the rate of vertical transmission was significantly higher in vaginally delivered infants

than in those delivered by cesarean section (32% vs 6%; $P < 0.05$).³⁶

Recommendations to decrease vertical transmission rates of chronic viral hepatitis.

- For pregnant women chronically infected with HBV:

1- HBsAg screening

Testing for the hepatitis B virus (HBsAg) is generally a standard, routine test performed on all pregnant women at or before her first pregnancy visit (usually before about 12 to 14 weeks of the pregnancy).^{37,38}

2- Management of infants born to women who are HBsAg positive

An unvaccinated baby whose mother is a hepatitis B carrier has up to a 40% chance of becoming infected with the virus during the first 18 months of their life, of which up to 90% can become a long term carrier and be infectious to others, as well as being at risk of liver disease and liver cancer in later life.

Therefore, all infants born to HBsAg positive women should receive hepatitis B vaccine and Hepatitis B Immunoglobulin (HBIG) (0.5 mL) \leq 12 hours of birth, administered at different injection sites.^{39,40}

Just to remember, HBIG provides passively acquired anti-HBs and temporary protection (i.e., 3-6 months) when administered in standard doses. The vaccine series should be completed according to a recommended schedule for infants born to HBsAg-positive mothers. The final dose in the vaccine series should not be administered before age 24 weeks (164 days).¹

For preterm infants weighing $< 2,000$ g, the initial vaccine dose (birth dose) should not be counted as part of the vaccine series because of the potentially reduced immunogenicity of hepatitis B vaccine in these infants; 3 additional doses of vaccine (for a total of 4 doses) should be administered beginning when the infant reaches age 1 month.³⁸

The hepatitis B vaccination can be delayed more than 24 hours after the baby's birth but definitely needs to be given before the baby is 7 days old.

Although not indicated in the manufacturer's package labeling, HBsAg containing combination vac-

cines may be used for infants aged ≥ 6 weeks born to HBsAg positive mothers to complete the vaccine series after receipt of a birth dose of single-antigen hepatitis B vaccine and HBIG.³⁸

A recent meta-analysis that evaluated the effects of hepatitis B vaccine and immunoglobulin in newborn infants of mothers positive for hepatitis B surface antigen, showed that there was no significant difference between recombinant vaccine and plasma derived vaccine on hepatitis B infections (relative risk 1.00, 95% CI 0.70 to 1.42).¹ However, more infants who received recombinant vaccine achieved antibody levels to hepatitis surface antigen > 10 IU/L.

Unfortunately, failure to postnatal immunoprophylaxis for hepatitis B has been reported, and specific allelic mutations in maternal HBV and level of maternal viremia were potential predictors of vertical breakthrough infection.¹⁸ Actually, it seems that S variants emerge or are selected under the immune pressure generated by the host or by administration of hepatitis B immune globulin and hepatitis B vaccination.⁴¹

- For pregnant women chronically infected with HCV:

In recent years, the testing for hepatitis C during pregnancy (anti-HCV) has become increasingly accepted as 'routine' by many maternity caregivers, along with testing for hepatitis B.

However, in some places, only women considered 'at risk' is tested. For example, women with a history of using intravenous drugs, hemodialyzed and hemophiliacs patients, history of transfusions before HCV screening or having tattoos or body piercing. Thus, testing for hepatitis C is not compulsory and some women do decline it if they do not wish to be tested. But, in general terms, screening for HCV infection needs to be mandatory to women with risk factors.⁴²

Maternal HCV-RNA testing should be required in prospective studies of perinatal HCV transmission, and analyses should be restricted to HCV-RNA positive mothers or stratified by HCV RNA status.¹⁹

Recommendations for screening and follow-up of infants born to HCV infected mothers include anti-HCV testing at age > 15 months or nucleic acid testing on 2 occasions between ages 2 and 6 months

Table III. Summary of recommendations to decrease vertical transmission rates of chronic viral hepatitis.

| | HBV | HCV |
|--|--|--|
| Type of delivery: elective cesarean | Not recommended | Not recommended |
| Breast-feeding | Encouraged (with appropriate immunoprophylaxis) | Encouraged |
| Vaccination to new-born | Compulsory: HBV vaccine + HBIG | Not available |
| Viral test screening | HBsAg screening (at or before their first pregnancy visit) | Anti-HCV screening (particularly high risk groups) |
| Antiviral therapy | Lamivudine (last month of pregnancy) | Contraindicated |

(National Institutes of Health Consensus Development Conference Statement. Management of hepatitis C: 2002, available at: <http://consensus.nih.gov/2002/2002HepatitisC2002116.html.htm>).

Finally, in *Table III* can be seen a summary of recommendations to decrease vertical transmission rates of chronic viral hepatitis.

Which is the role of breast-feeding in transmission of hepatitis virus to infants born to chronic infected mothers?

For pregnant women chronically infected with HBV

Mothers who carry the hepatitis B virus are encouraged to breastfeed their babies. However, it is recommended that the baby breastfeeds after the administration of the HBIG but not necessarily before the first hepatitis B vaccination (HBV).^{40,43}

As HBV transmission through breast milk has been reported in some studies,^{44,45} several groups disagree and do not recommend breast-feeding on the basis of published data.^{46,47}

Finally, as a general advice, it is recommended to explain the mothers that when breast-feeding she should take good care of her nipples, ensuring proper latch-on and allowing the nipples to dry before covering to avoid cracking or bleeding, having in mind that HBV is commonly passed by blood-to-blood routes.

For pregnant women chronically infected with HCV

Several recent studies demonstrate no increased risk of HCV transmission attributable to breast-feeding. All major health organizations (i.e. World Health Organization, Centers for Disease Control, National Institutes of Health and American Academy of Pediatrics) recommend or support breastfeeding by hepatitis C carrier mothers. As the risk of vertical transmission of HCV appears to increase with HCV-RNA titer, one approach would be to breastfeed if the mother's HCV-PCR is negative or low titer, and recheck the mother's titer periodically (actually, a not practical approach). Besides, HCV antibodies and HCV-PCR should be followed periodically in the infant during the first 12 to 18 months of life whether or not the infant is breastfed.⁴⁸

Lastly, detection of HCV-RNA in colostrum or breast milk was not related to HCV RNA level in maternal serum.¹⁹ But, a study that enrolled seventy-three infants of 63 anti-HCV positive and anti-HIV negative mothers in Spain showed that breast milk HCV-RNA was negative in non-viremic mothers and positive in 20% of the viremic mothers.⁴⁹

In this regard, some authors advice that women with high viral loads, should not breast-feed to avoid the risk of viral transmission through breast-feeding.⁵⁰

Should antiviral treatment of pregnant women with chronic hepatitis C be delayed until after they have given birth?

Given the frequency of side effects, in the case of pregnant women with chronic HCV infection, it seems preferable not to begin combined therapy with interferon and ribavirin until after delivery. Besides, because interferon has antiproliferative activity, its effects on the fetus are a concern. Despite warnings to the contrary, some patients may become pregnant while on interferon therapy for hepatitis C and even though a number of case reports in the past have suggested relative safety of alpha-interferons during pregnancy with little or no effect on the fetus⁵¹ a case of neonatal lupus and intrauterine growth restriction following alpha-interferon therapy during pregnancy was reported.⁵²

Interestingly, endogenous interferon may play a role in maintaining pregnancy.⁵³ During pregnancy, interferon-alpha is produced locally in the fetoplacental unit and in vitro studies have shown that interferon induces a three-fold production of human chorionic gonadotropin, a hormone that maintains the corpus luteum early in the pregnancy.⁵⁴

Lastly, there are no reports of interferon acting as an abortifacient in humans and there were no reported abortions in the 24 cases revised by Trotter, et al.⁵⁵

In general, pregnant women are usually advised to stop taking the medication during pregnancy; and women should not become pregnant while on interferon and ribavirin combination therapy.

Regarding ribavirin, the drug has a high risk of causing birth defects in the unborn baby and women are advised not to conceive for at least 6 months after stopping the ribavirin medication and should not breastfeed if taking ribavirin. As a result, ribavirin is designated FDA Pregnancy Category X.

In fact, it is recommended by the manufacturer that a woman of childbearing age use effective contraception during treatment and for 6 months after treatment ends because of the high risk for birth defects in the fetus. In the same way, mothers taking antiviral medication should not breast feed because of the potential for an adverse reaction from the drug in their infant. In effect, a group of scientific advisors to the Ribavirin Pregnancy Registry, (<http://www.ribavirinpregnancyregistry.com>) maintains a registry of pregnancy-related exposures and advises all women to wait 6 months following discontinuation of ribavirin before attempting to get pregnant. The Board strongly encourages colleagues to prospectively (before the outcome of the pregnancy is known) enroll individuals with pregnancy exposures to ribavirin in the Registry as early in pregnancy as possible.

The extensive accumulation of ribavirin in erythrocytes and other tissue and its slow clearance rate raise the possibility that it could accumulate in sperm in concentrations high enough to induce defects. In animal studies, ribavirin produced changes in sperm at sub-clinical dos-

es. Another mechanism by which ribavirin treatment could theoretically affect embryo development is by being transmitted through seminal fluid.⁵⁶

It is also stated in the level of the medication that female patients and female partners of male patients being treated with ribavirin must not become pregnant during treatment and for 6 months after treatment has stopped, and it is explicitly advised the use of any secure use of birth control (particularly condom with spermicidal).

In spite of these recommendations, if an unexpected pregnancy occurs while the father is receiving this therapy, there is no medical indication for terminating the pregnancy.^{57,58}

Does antiviral maternal therapy prevent vertical transmission of hepatitis B virus?

The fact that vertical transmission of hepatitis B virus may occasionally occur despite vaccination of the child has prompted to physicians to treat viremic patients with nucleosides analogues to prevent mother-to-child transmission.

As regards, some authors observed that in highly viremic HBsAg positive mothers, reduction of viremia by lamivudine therapy in the last month of pregnancy could be an effective and safe measure to reduce the risk of child vaccination breakthrough.^{59,60} Moreover, no side effects were observed neither in the mother nor in the babies, observation that had been made before when studying the safety, pharmacokinetics and antiretroviral activity of lamivudine alone and in combination with zidovudine in pregnant women infected with human HIV-1.⁶¹

Nonetheless, in spite of the optimum maternal therapy and neonatal vaccination above reported with encouraging results in controlling vertical transmission, some other authors affirm that lamivudine therapy might not prevent perinatal transmission.⁶² Finally, I wish to introduce a note of caution concerning the use of lamivudine or any other nucleoside during the first trimester of pregnancy, particularly taking into account the possible lethal effects during the embryogenesis.⁶³

Is there any role of chronic viral infection on pregnancy outcome, neonatal morbidity and teratogenic effect?

As a general rule, there is no reason to occur adverse pregnancy outcomes in compensated chronic HBV carriers. However, there has been case reports and studies indicating an increased incidence of maternal and neonatal morbidity in HBV infection, for instance, premature delivery before 34 weeks, raised incidence of antepartum hemorrhage,⁶⁴ fetal distress, and meconium peritonitis.⁶⁵⁻⁶⁷ Additionally, it has been suggested the association of maternal hepatitis B surface antigen carriers and chromosomal abnormalities in their newborns,⁶⁸ an observation barely replicated. One interesting finding is the association between gestational dia-

betes mellitus and HBsAg carrier status observed by Lao et al⁶⁹ and Tse K et al,⁶⁴ both in Chinese women. The authors hypothesize that this event may be explained by the increased level of pro-inflammatory cytokines induced by chronic HBV infection, and in particular by the effect of the tumor necrosis factor α .

In the case of HCV, no adverse effect on pregnancy outcome was observed in terms of gestational age, Apgar score and baby weight.⁷⁰⁻⁷²

Alternatively, Paternoster et al. reported an elevated occurrence of intrahepatic cholestasis of pregnancy (ICP) in HCV positive women. Therefore, the authors recommend that during the third trimester of pregnancy, if ICP appears, it should be an indication to investigate the HCV status of the patient.⁷³

Counseling about the risk associated with amniocentesis, assisted reproductive technology and prenatal risk screening in pregnant women with chronic hepatitis. Some information for the reproduction team

Obstetrician and gynecologists are important providers of primary health care to pregnant women with chronic liver disease. This last part of the review aims to summarize some aspects of the daily clinical practice of Obstetrician and gynecologists targeted to risk and concerns about chronic viral hepatitis during pregnancy.

For example, knowledge of the maternal HBeAg status is valuable in the counseling of risks associated with amniocentesis in chronic HBV carriers. It was shown that the risk of fetal hepatitis B infection through amniocentesis is low⁷⁴ and genetic amniocentesis did not increase the risk of intrauterine HBV infection. However, for those women infected with hepatitis B or hepatitis C who insist on amniocentesis, every effort should be made to avoid inserting the needle through the placenta.³⁴ Additionally, amniocentesis in women infected with hepatitis C does not appear to significantly increase the risk of vertical transmission, but women should be counseled that very few studies have properly addressed this possibility.⁷⁵ Besides, the presence of intra-amniotic bleeding during the procedure may be a risk factor for the baby infection.

Another concern is about cross-contamination between patients during assisted reproductive techniques. Hepatitis B contamination has been described during artificial insemination⁷⁶ as well as HCV cross-contamination between patients during assisted conception⁷⁷ and demonstrated as possible during artificial insemination.⁷⁸

As the capacity for transmission of hepatitis B infection by semen is well recognized, screening of semen donors should be a routine practice for avoiding the potential for transmission by artificial insemination.

Also, medical assistance to procreation in a couple with one of the parents having viral hepatitis raises the issue of the transmission of infection to the baby. As we do

not yet know if an excess risk of vertical transmission of HCV and HBV exists during assisted reproductive techniques, universal recommendations should be followed and it is also recommended that infertile patients be screened before assisted reproductive techniques.⁷⁸

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