# SOGP GUIDELINE OF VIRAL HEPATITIS IN PREGNANCY

Adapted for Pakistan from the Green top RCOG guideline No: 20a, 2006

By the Guideline Committee of SOGP through consensus & literature review

Reviewed by: The executive Body of SOGP

Endorsed by: The CPSP

## 1. PURPOSE AND SCOPE

Viral Hepatitis is the commonest cause of liver dysfunction in pregnancy, worldwide.

Hepatitis may be caused by numerous viruses, drugs, or toxic chemicals .The most common viral agents causing hepatitis in pregnancy are Hepatitis A virus, Hepatitis B virus, Hepatitis C virus & Hepatitis E virus

Pregnancy does not affect the course of hepatitis unless a woman has hepatitis E, which can worsen severely in some cases.

## 2. HEPATITIS A IN PREGNANCY:

The primary mode of transmission is the fecal/oral route .Symptoms are fever, chills, anorexia, nausea and vomiting and then by the onset of dark urine, pale stools, jaundice and hepatomegaly. It is diagnosed by checking the levels of **IgM anti-HAV** anti-bodies (which can persist for months after the infection.)

Mother to Child Transmission (MTCT) of HAV is very rare. If the newborn is exposed, the infection is usually mild and they will have a life long immunity to the disease.

If a pregnant woman is exposed (such as when travelling or by contact with known carriers) She should be given immune gamma globulin (IG) to help protect her from getting the disease.

Vaccination in pregnancy is not recommended at present

## HEPATITIS B IN PREGNANCY

Hepatitis B is one of the most highly transmitted forms of hepatitis from mother to child. All women who are found to be HBsAg positive during pregnancy should undergo appropriate testing, assessment and referral. Although the mother will usually become jaundiced during the acute stage, some women have no symptoms of hepatitis. Screening of all women for hepatitis B during the first prenatal visit is recommended.

The virus is highly contagious and the risk that the newborn infant will develop hepatitis B is 10 to 20% if the mother is positive for **HbsAg** and as high as 90% if she is also positive for **HbeAg.**

Vaginal delivery should be the aim, as there is limited research on the best mode of delivery of Hep-B positive women.

If the pregnant woman tests positive during her antenatal visits for hepatitis B she should receive hepatitis B immunoglobulin and the new born should receive hepatitis B vaccine at 1 week, 1 month and 6 months after birth. This reduces the risk of infection to the infant to a range of 0 to 3%

Symptoms are fever, chills, anorexia, nausea and vomiting and then by the onset of dark urine, pale stools, jaundice and hepatomegaly.

Diagnosis is confirmed by checking the levels of HBsAg and HBc IgM.

## HEPATITIS C IN PREGNANCY

Hepatitis C virus can develop into chronic infection leading to cirrhosis and hepatocellular carcinoma. Most women become pregnant aged between 20 to 40 years, which is also the age group in which the incidence of hepatitis C infection is rising most rapidly.

Women more at risk for hepatitis C are those who are exposed to blood transfusions, contaminated needles or injected drug use, medical procedures in resource poor settings or tattooing.

Although regarded as a blood borne infection among adults, mother to child transmission is the leading cause of hepatitis C infection among infants and children.

The risk of a pregnant woman passing the hepatitis C virus to her unborn child has been related to the levels of quantitative **RNA** levels in her blood and also whether she is also **HIV+ve**.

Symptoms are fever, chills, anorexia, nausea and vomiting and then by the onset of dark urine, pale stools, jaundice and hepatomegaly.

Diagnosis is confirmed by checking the levels of **Anti HCV.**

**HEPATITIS E IN PREGNANCY**

Hepatitis E virus (HEV) causes an acute, usually self limiting hepatitis. It can lead to fulminant hepatitis which happens more frequently among pregnant women than any other subgroup.

Major causes are water borne epidemics associated with poor sanitary conditions (rainy season or flooding).

Liver injury coincides with marked **ACT** elevation and appearance of **anti-HEV Igm**.

Trans-placental transmission of HEV has been documented by specific HEV Igm in cord blood and virus isolation by PCR resulting in neonatal massive hepatic necrosis and death. However infants generally recover from in Utero infection.

Symptoms are fever, chills, anorexia, nausea and vomiting and then by the onset of dark urine, pale stools, jaundice and hepatomegaly.

HEV infection does not cause chronic hepatitis, cirrhosis or hepatocellular carcinoma.

Pregnant women during second and third trimesters are more susceptible to infection by HEV and progression to fulminant hepatic failure.

Diagnosed by checking the levels of **HEV IgM, IgG.**

## 3. DIFFERENTIAL DIAGNOSIS:

- Acute fatty liver of pregnancy.
- Cholelithiasis and Cholecystitis.
- Autoimmune hepatitis (AIH).
- Cholestasis of pregnancy.

## 4. Management

Bed rest should be instituted during the acute phase of illness. If nausea, vomiting, or anorexia is prominent, intravenous hydration and general supportive measures are instituted.

All hepatotoxic agents should be avoided.

There are increased risks for premature delivery and still birth.

Immunoglobulin prophylaxis should be given to pregnant women within 2 weeks of exposure to hepatitis A.

Hepatitis B vaccine also should be administered to HBsAg-negative patients.

Referral of chronic hepatitis carriers to liver disease experts

Routine prenatal screening of all pregnant women for hepatitis B & hepatitis C.

Immunoprophylaxis of newborns born to hepatitis B carries with hepatitis B immune globulin & hepatitis B vaccine within 12hrs of birth.

Vaccination of infants, and at-risk individuals with hepatitis B vaccine, particularly healthcare workers.

Considerations for amniocentesis, route of delivery and breast feeding in women infected with hepatitis.

All women presenting for preconception counseling should have their immunization records reviewed and updated identification of vaccination gaps should lead to vaccination ideally prior to conception.

Hepatitis B is a preventable disease and all at risk individuals should be vaccinated. All infants should receive the hepatitis B vaccine series as a part of the recommended childhood immunization schedule.

**BREAST FEEDING**

Breast feeding is not contraindicated in women with hepatitis A virus (HAV) infection with appropriate hygienic precautions, in those chronically infected with hepatitis B, if the infant receives HBIG (passive prophylaxis) & vaccine (active prophylaxis) or in women with hepatitis C virus (HCV) infection. Breast feeding does not appear to transmit the hepatitis B virus (World Health Organization). Recommendations that the infant be re vaccinated are given as additional insurance against infection. There is no evidence that breast-feeding spreads HCV. An infected mother should however avoid breastfeeding if her nipples are cracked and bleeding.

**Breast feeding is not contraindicated in any subtypes of hepatitis**

**MODE OF DELIVERY**

Route of delivery has not been shown to influence the risk of vertical HCV transmission and cesarean delivery should be reserved for obstetric indications in women with HCV infection.

The risk of transmission of hepatitis B with **amniocentesis** is low.

Maternal immunization may also affect fetal and neonatal well being, as efficient placental transfer of maternal antibodies to the fetus starts at 32 weeks, conferring protection for the first six months of life.

**General diagnostic tests**:

- Serum transaminase levels and bilirubin levels.

**Specific diagnostic/screening tests**:

- Hepatitis A virus (HAV) IgM antibodies.
- Hepatitis B virus (HBV) surface antigen (HbsAg) HBV surface IgG antibody (anti HBS).
- Hepatitis C antibody (anti HCV).
- Hepatitis D virus (HDV) antigen in hepatic tissue; IgM antibody to HDV.
- Hepatitis E virus-specific antibodies.

About 4% infants born to HCV-infected women become infected. While there is no preventive treatment, there is a high probability of the babies ridding themselves of the HCV in the first 12 months.

In a mother who also has HIV, the rate of transmission can be as high as 19%. There are currently no data to determine whether antiviral therapy reduces perinatal transmission. **Ribavirin and interferons are contraindicated during pregnancy**.

Avoiding fetal scalp monitoring and prolonged labor after rupture of membranes may reduce the risk of transmission to the infant.

HCV antibodies from the mother may persist in infants until 15 months of age. If an early diagnosis is desired, testing for HCV RNA can be performed between the ages of 2 and 6 months, with a repeat test done independent of the first test result. If a later diagnosis is preferred, an anti-HCV test can performed after 15 months of age.

Most infants infected with HCV at the time of birth have no symptoms and do well during childhood.

## ADDITIONAL RECOMMENDATIONS

Current guidelines strongly recommend that hepatitis C patients be vaccinated for hepatitis A and B if they have not yet been exposed to these viruses, as infection with a second virus could worsen their liver disease.

Alcoholic beverage consumption accelerates HCV associated fibrosis and cirrhosis, and makes liver cancer more likely; insulin resistance and metabolic syndrome may similarly worsen the prognosis. There is also evidence that smoking increases the fibrosis rate.

**UK guidelines for the initial management of hepatitis B infection** and **UK guidelines for the management of babies born to women who are HbsAg Positive** (British Viral Hepatitis Group):

**The United Kingdom National Guideline on the Management of the Viral Hepatitides A, B & C 2008** (Clinical Effectiveness Group British Association of Sexual Health and HIV) says:

"Vertical transmission (mother to infant) of infection occurs in ninety percent of pregnancies where the mother is hepatitis B e antigen positive and in about ten percent of surface antigen positive, e antigen negative mothers. Most (>90%) of infected infants become chronic carriers.

Infants born to infectious mothers are vaccinated from birth, usually in combination with Hepatitis B specific Immunoglobulin 200 i.u. i.m. (Ia, A). This reduces vertical transmission by ninety percent.

There is some evidence that treating the mother in the last month of pregnancy with **lamivudine** may further reduce the transmission rate if she is highly infectious (HBV DNA >= 1.2 x 10 9 geq/ml) (III, C), but this needs to be further substantiated. Hepatitis B may exacerbate after the end of pregnancy"

**EASL Clinical Practice Guidelines: Management of chronic hepatitis B** (European Association for the Study of the Liver):
"Lamivudine, adefovir and entecavir are listed by the FDA as pregnancy category C drugs, and telbivudine and tenofovir as category B drugs. These classifications are based on the risk of teratogenicity in preclinical evaluation. There is a considerable body of safety data in pregnant HIV-positive women who have received tenofovir and/or lamivudine or emtricitabine. Recent reports suggest that lamivudine therapy during the last trimester of pregnancy in pregnant HBsAg-positive women with high levels of viremia reduces the risk of intra-uterine and perinatal transmission of HBV if given in addition to passive and active vaccination by HBIg and HBV vaccination. Tenofovir or tenofovir with emtricitabine or entecavir could be considered. Although apparently safe, these protocols require further confirmation (B2). HBV-infected women should be monitored closely after delivery as exacerbations of chronic hepatitis B may occur"

**American College of Obstetricians and Gynecologists**, Viral hepatitis in pregnancy
"The risk of transmission of hepatitis B associated with amniocentesis is low"

(Evidence level IV)

**Cochrane reviews** are currently being prepared for the effectiveness of three interventions in the prevention of hepatitis B in infants: lamivudine (Mumtaz), Hepatitis B immunoglobulin (Eke) or vaccination (Sangkomkamhang)

**References:**

American College of Obstetricians and Gynecologists. Viral hepatitis in pregnancy. Practice Bulletin 86; Obstet Gynecol 2007 Oct; 110(4):941-56.

British Viral Hepatitis Group. UK guidelines for the initial management of hepatitis B infection, London 27 June 2008. BVHG Consensus Statement –UK guidelines for the management of babies born to women who are HbsAg Positive

British Viral Hepatitis Group. UK guidelines for the initial management of hepatitis B infection, London 27 June 2008. BVHG Consensus Statement –Initial Testing and Referral of Individuals who are HBsAg Positive

Clinical Effectiveness Group British Association of Sexual Health and HIV /United Kingdom National Guideline on the Management of the Viral Hepatitides A, B & C 2008

European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Management of chronic hepatitis B. Journal of Hepatology 50 (2009) 227–242

Forthcoming Cochrane reviews:

Eke Ahizechukwu C; Eke Uzoamaka A, Uchenna Eleje. Hepatitis B immunoglobulin during pregnancy for the prevention of mother to child transmission of hepatitis B virus. Cochrane Database of Systematic Reviews: Protocols 2010 Issue 6 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD008545

Mumtaz Khalid, Ahmed Umair Syed, Zuberi Nadeem F, Salamat Sumaira, Jafri Wasim. Lamivudine during pregnancy for preventing hepatitis B virus infection in newborns. Cochrane Database of Systematic Reviews: Protocols 2010 Issue 9 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD008718

Sangkomkamhang Ussanee S, Lumbiganon Pisake, Laopaiboon Malinee. Hepatitis B vaccination during pregnancy for preventing infant infection. Cochrane Database of Systematic Reviews: Protocols 2009 Issue 3 John Wiley & Sons, Ltd Chichester, UK DOI: 10.1002/14651858.CD007879

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**Classification of evidence levels**

Ia Evidence obtained from meta-analysis of randomized controlled trials.

Ib Evidence obtained from at least one randomized controlled trial.

IIa Evidence obtained from at least one well-designed controlled study without randomization.

Ibis Evidence obtained from at least one other type of well-designed quasi-experimental study.

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

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**These guidelines are not dictating an exclusive course of treatment or procedure. Variations in practice may be based on the needs of the individual patient, resources and limitations unique to the institution or type of practice.**