

# Pregnancy Outcome in Viral Hepatitis

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## ABSTRACT

**Introduction:** Hepatitis in pregnancy is an important medical disorder seen more often in developing countries than in developed ones. Viral hepatitis is a major public health problem in India. Hepatitis in pregnancy is commonly associated with abortion, premature delivery, postpartum hemorrhage, coagulation defect, obstetric shock, coma, death and increased perinatal mortality and morbidity. This study was carried out to know the effect of viral hepatitis on pregnancy and to study its maternal and fetal outcome.

**Materials and methods:** This prospective clinical study was conducted in the Department of Obstetrics and Gynecology NKP Salve Institute of Medical Sciences and Research Centre and Lata Mangeshkar Hospital, Nagpur, from January 2010 to December 2012. All the antenatal cases attended Obstetrics and Gynecology Department were investigated for HBsAg and looked for any symptoms and signs suggesting hepatitis like fever, jaundice, nausea, vomiting. If present, they were admitted and further investigated to detect viral hepatitis. Patients were counseled for follow-up and strict hospital delivery. Patients with viral hepatitis were analyzed for the effect on pregnancy, maternal and fetal outcome.

**Results:** There were total 30 cases of viral hepatitis 24 (80%) cases were HBsAg positive, but all were asymptomatic 6 (20%) cases were hepatitis E positive. No HAV, HCV, HDV and hepatitis G infected cases were detected in our study. Maternal and fetal morbidity was significantly higher in hepatitis E infected women. Fetal mortality was observed in one case.

**Conclusion:** Pregnancy with viral hepatitis requires early diagnosis, hospitalization and treatment. In the present study hepatitis E was found to be the chief etiological agent associated with increased maternal morbidity, and high fetal morbidity and mortality.

**Keywords:** Viral hepatitis, Pregnancy outcome, Liver function test.

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## INTRODUCTION

Hepatitis in pregnancy is an important medical disorder seen more often in developing countries than in developed ones. Viral hepatitis caused by different type of viruses A, B, C, D, E and G is a major public health problem in India. Hepatitis in pregnancy is commonly associated with abortion, premature delivery, postpartum hemorrhage, coagulation defect, obstetric shock, coma, death and increased perinatal mortality and morbidity.

Hepatitis B virus infection in India is of intermediate endemicity with nearly 4% of the population being chronic hepatitis B virus carriers that is about 40 millions people. Most of them are asymptomatic, but they are at increased risk of liver cirrhosis and hepatocellular carcinoma. Over 50% of these carriers are believed to have acquired their infection vertically from their mother through mother to child transmission (MTCT), and horizontal transmission in the perinatal period and in early childhood. Vertically acquired HBV infection frequently (>90%) becomes chronic. Strategies to prevent MTCT would go a long way in global control of HBV infection, and so associated morbidity and mortality. Thus, chronic HBV infection during pregnancy is an important opportunity to interrupt perinatal transmission of HBV.<sup>1-3</sup>

HEV infection is the most frequent cause of acute sporadic and epidemic hepatitis in India, transmitted through contaminated water. It is a major cause of acute hepatitis and acute liver failure which is severe in pregnant women. Prevention is possible through public health measures such as clean water supply, improved sanitation and public education.<sup>4</sup>

## MATERIALS AND METHODS

This prospective clinical study was conducted in the Department of Obstetrics and Gynecology NKP Salve Institute of Medical Sciences and Lata Mangeshkar Hospital, Nagpur (Maharashtra), from January 2010 to December 2012. The study was approved by the Institutional Research and Ethics Committee. Informed consent was taken. All the antenatal cases attended Obstetrics and Gynecology Outpatient Department were tested for HBsAg (Australia Antigen), and if found positive were included in the study. Pregnant women with symptoms of hepatitis like fever, icterus, nausea, vomiting were admitted to find out the cause. A detailed history, clinical examination, laboratory tests complete blood count, liver function test, renal function test, coagulation profile, ultrasonography was done. All pregnant women with viral hepatitis were included in the study. Patients were counseled for regular follow-up and strict hospital delivery. At the time of hospitalization for delivery, again a detailed history, general, systemic and obstetrical examination was done. Investigations repeated as and when required. Mode of delivery, indication for cesarean section, complications if any were noted. Neonatal weight and maturity was noted. Need for admission in premature baby unit or Neonatal Intensive Care Unit was recorded.

Maternal outcome was noted in terms of the mode of termination of pregnancy, maternal complication and maternal end result. Fetal outcome was assessed by fetal weight, prematurity, intrauterine death, need for admission to premature baby unit and Neonatal Intensive Care Unit.

All the infants born to HBsAg positive women were given both hepatitis B immunoglobulin (0.05 to 0.07 ml/kg) and hepatitis B vaccine 1.0 ml (20 µg/ml) within first 24 hours of birth. The infant should receive the second and third dose of vaccine after 1st and 6th month respectively.<sup>5</sup> HBsAg and anti-HBs to be tested at the age of 9 months.

## RESULTS

Total 30 women were studied. Most women were between the age group of 20 and 30 years. They mainly belonged to educated category, homemaker, from lower middle socioeconomic status. Twenty-two women (73.3%) belonged to rural area and eight women (26.6%) belonged to urban area. Twenty-four women (80%) were HBsAg positive but asymptomatic. Most of them were admitted with amenorrhea 9 months with labor pain. Six women (20%) were hepatitis E positive symptomatic. Most of them were admitted in second and third trimester with deranged liver function test. No other type of viral hepatitis was reported in our study.

Out of 24 HBsAg positive (80%) women, 19 women delivered by normal vaginal route. Postpartum period was uneventful except for one woman who developed atonic postpartum hemorrhage just after delivery, which was controlled by injection methergin, injection prostidin, and needed 3 units of blood transfusion. Five women were delivered by cesarean section. Indication for cesarean section was cephalopelvic disproportion with oligohydramnios, severe oligohydramnios, fetal distress, postdated pregnancy with previous cesarean section. All women were asymptomatic having normal pathological test. No women needed referral to medicine unit and no intensive care unit admission (Table 1).

Table 1 showing 6 women (20%) were hepatitis E positive, showing symptoms and signs of hepatitis. They reported at

2nd and 3rd trimester of pregnancy with deranged pathological tests. Out of 6 cases of hepatitis E positive women two had preterm vaginal delivery (31 weeks 1 day and 33 weeks 3 days gestational age each). Both women presented with severely deranged liver function test, fever, icterus. Two women who were 29 weeks gestation had severely deranged liver function test and jaundice, were transferred to medicine unit for further management but they discharged against medical advice from medicine unit and lost to follow-up. One woman with deranged liver function test and 33 weeks pregnancy had accidental hemorrhage. Cesarean section was performed, baby was intrauterine dead. Mother needed intensive care unit admission. One woman needed elective cesarean section for cephalopelvic disproportion, had average for gestational age baby. Postoperative period was uneventful.

Table 2 showing fetal outcome in study participants. In HbsAg positive women, out of 19 women who delivered by normal vaginal route 15 babies were average for gestational age and 4 babies were small for gestational age. Five women who delivered by cesarean section 3 babies were average for gestational age and 2 babies were small for gestational age. No baby was preterm so no premature baby unit admission. No baby needed neonatal intensive care unit admission. No intrauterine death was seen in HbsAg positive women.

Out of 6 babies with Hepatitis E positive women only one baby was average for gestational age who delivered by elective cesarean section for cephalopelvic disproportion. Two babies were preterm 31 weeks 1 day and 33 weeks 3 days gestational age each. Both premature babies needed premature baby unit admission for low birth weight 1.15 and 1.75 kg respectively. One baby was intrauterine dead, who delivered by cesarean section as mother had accidental hemorrhage. Two women lost to follow-up undelivered in Hepatitis E positive cases (Table 2).

## DISCUSSION

Viral hepatitis in pregnancy is the most common cause of jaundice in pregnancy. The outcome is usually benign except in viral hepatitis E. Viral hepatitis in pregnancy may not always affect the outcome of pregnancy; transmission to the newborn is always a concern. Diagnosis of viral hepatitis during pregnancy is not different from the diagnosis in the non-pregnant state. Reports from Europe and US have shown the course of viral hepatitis during pregnancy to be in no way

**Table 1:** Distribution of study participants according to maternal outcome

| Maternal outcome   | HBsAg positive<br>80% (n = 24) | Hepatitis E positive<br>20% (n = 6) |
|--|--------------------------------|-------------------------------------|
| Vaginal delivery   | 19                             | 2                                   |
| Cesarean section   | 5                              | 2                                   |
| Referred to medicine<br>(lost to follow-up, undelivered) | 0                              | 2                                   |
| Intensive care unit admission                            | 0                              | 1                                   |
| Deranged pathological tests<br>and symptomatic           | 0                              | 6                                   |

**Table 2:** Distribution of study participants according to fetal outcome

| Fetal outcome                                   | HBsAg positive (no. of cases 24) |                  | Hepatitis E positive<br>(no. of cases 6) |
|---|----------------------------------|------------------|--|
|   | Vaginal delivery                 | cesarean section |  |
| Average for gestational age                     | 15                               | 3                | 1  |
| Small for gestational age                       | 4                                | 2                | 0  |
| Preterm baby with premature baby unit admission | 0                                | 0                | 2  |
| Intrauterine death                              | 0                                | 0                | 1  |
| Lost to follow-up undelivered                   | 0                                | 0                | 2  |

different from nonpregnant women. However, studies carried out in India, Iran and Africa have found the incidence of fulminated hepatitis to be higher in pregnancy. Malnutrition superimposed on the normal demands of pregnancy and inversion of T and B lymphocytes in early pregnancy have been postulated to be the contributing factors.<sup>6</sup>

In our study hepatitis B virus (HBV) infection during pregnancy does not appear to increase the maternal and fetal mortality and morbidity. As in one large study they compared 824 HBsAg positive mother to 6281 HBsAg negative control mothers found no difference in rate of preterm delivery, birth weight, neonatal jaundice, congenital anomalies or perinatal mortality. In a population based retrospective review of data from 186,619 deliveries in Israel; 749 hepatitis B or C seropositive pregnant women had higher rates of preterm deliveries, premature rupture of membranes, placental abruption, labor induction and cesarean deliveries as also of perinatal mortality, congenital malformation and low birth weight.<sup>7</sup>

Hepatitis B virus infection is a global problem and world has 350 millions carriers of chronic hepatitis B. Over 50% of these have acquired their infection vertically from their mothers, mother to child transmission. (MTCT). Majority (90%) of vertically acquired infection results into chronic infection, due to induction of an immune tolerant state. Hence, management of chronic HBV during pregnancy and strategies to prevent MTCT would go a long way in global control of HBV infection and the morbidity and mortality associated with it.<sup>7</sup>

The American Association for the Study of Liver Disease (AASLD) recommends that all pregnant women be screened for HBsAg during the first trimester, even if previously vaccinated or tested. Screening allows for identification of infants requiring immunoprophylaxis with HBV vaccine and hepatitis B immunoglobulin (HBIG), antiviral treatment of pregnant carriers if indicated, and counseling of sexual and household contacts. The HBsAg positive pregnant women should be counseled to inform their obstetrician so that immunoprophylaxis can be administered to the newborn immediately after delivery. Women who test negative for HBsAg and are at risk of acquiring HBV infection should be immunized during pregnancy. The hepatitis B vaccine is considered safe during pregnancy with no adverse reactions reported. Proof of absent immunity (absence of anti- HBs) is not required before vaccination. Maternal high HBV DNA and HBsAg positivity are important risk factors for MTCT. Women having these risk factors may be considered for one of the following measures to reduce the risk of MTCT. Use of antiviral therapy (lamivudine, telbivudine or tenofovir) in third trimester, use of 3 doses of HBIG in pregnancy (200 IU at 28,32, and 36 weeks), use of elective cesarean section before the onset of labor. Breastfeeding of infant is recommended, however mother should stop antiviral therapy

to limit the exposure of infants to these drugs. The American Congress of Obstetrician and Gynecologist (ACOG) and AASLD guidelines suggest that HBsAg positive mothers be referred for further medical evaluation so that those with liver disease can be identified and monitored frequently by a team of specialists. This should not be deferred to the postpartum period.<sup>7</sup>

In our study out of 30 cases, 24 were HBsAg positive but asymptomatic. They have less maternal and perinatal morbidity and mortality. Six were hepatitis E positive. In them high maternal morbidity and high perinatal morbidity and mortality was observed.

Most guidelines now recommend that infants born to HBsAg positive women should receive both HBIG and hepatitis B vaccine within 24 hours of birth, preferably in the delivery room. This should be followed by at least two more doses of hepatitis B vaccine within the first 6 months of life. Passive immunoprophylaxis with HBIG at birth followed by at least 3 doses of vaccine provides 90 to 95% protection from perinatal infection, and is superior in reducing MTCT than HBIG or vaccine alone. WHO recommends breastfeeding even for infants of HBsAg positive mothers in endemic areas where HBV vaccination may not be readily available.<sup>7</sup> In our center we followed this standard protocol.

Regarding the laboratory investigations in our study all the women with HBsAg positive asymptomatic pregnant women showed normal liver function test and coagulation profile. Whereas HBE positive women showed marked rise of total serum bilirubin level, raised liver enzyme levels, prolonged prothombin time and partial thromboplastin time. During two consecutive years of our study we did not find any other type of viral hepatitis during pregnancy apart from asymptomatic HBsAg and symptomatic HBE infection.

## CONCLUSION

Viral hepatitis specially hepatitis E is an important cause of maternal and perinatal morbidity and mortality. All pregnant women should be screened for HBsAg during the first trimester or as and when she comes for the first time for antenatal checkup, even if previously vaccinated or tested. They should be investigated to rule out chronic liver disease and cirrhosis. They might require special care during pregnancy and delivery. The risk of mother to child transmission is assessed and If required measures can be taken to reduce the risk.

As no specific therapy is capable of altering the course of acute hepatitis E infection, prevention is the most effective approach against the disease. Hospitalization is required for fulminant hepatitis and should be considered for infected pregnant woman. This is single hospital based study, multicentric hospital based studies should be conducted to get more information.

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