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Original Article

Fetomaternal Outcome in Viral Hepatitis in Pregnancy – A Tertiary Care Hospital-based Study

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Abstract

Background: The most common viral agents causing hepatitis in pregnancy are hepatitis A virus, hepatitis B virus, hepatitis C (non-A and non-B hepatitis virus), hepatitis E, hepatitis G, and Epstein-Barr virus. Delta agent hepatitis has also received increasing attention as a cause of hepatitis. Various authors have reported findings ranging from no difference in fetal/maternal outcome to nearly universal fatality. Interestingly, these different types of outcome are peculiar to certain geographical areas. Jaundice complicates 3–5% of pregnancies and is one of the important causes of maternal and neonatal morbidity and mortality worldwide. It is responsible for 10% of maternal deaths.

Objective: The aim of the study was to study the maternal and fetal outcome in viral hepatitis in pregnancy.

Materials and Methods: After admission, all patients had a thorough history and clinical examination. The period of gestation was calculated on the basis of last menstrual period and early ultrasound which ever was available. The blood sample was collected and was sent for biochemical studies for liver function test, coagulation profile, and serological tests for Immunoglobulin (Ig)M anti-hepatitis A virus, Hepatitis B surface antigen, IgM anti-Hepatitis E virus, and IgM anti-hepatitis C virus using commercially available ELISA kits.

Results: Indications for caesarean section were acute fetal distress in 23 (54.8%) and the other indications included oligohydramnios, color Doppler changes, cephalopelvic disproportion, non-progression of labor, intra uterine growth restriction, macrosomia, and malpresentation were seen in 6 (14.3%), 3 (7.1%), 3 (7.1%), 2 (4.8%), 2 (4.8%), 2 (4.8%), and 1 (2.4%) women, respectively. Thrombocytopenia was observed in 14 (3.33%) women and postpartum hemorrhage and hypoglycemia in 3 (7.1%) patients each. Normal birth weight was observed in 65 (97%) patients while as 2 (3%) babies were overweight. The mean birth weight was 2.73 ± 1.26 kg. There were 42 (62.7%) patients with 1 min Apgar >7 compared to 49 (73.1%) at 5 min Apgar score >7 days. Fetal outcomes such as NICU admission were observed in 16 (38.1%) NICU admission, low birth weight in 7 (16.7%), and 2 (4.8%) intrauterine deaths.

Conclusion: In the case of women with very high viremia, a non-negligible proportion of newborns can acquire the infection (probably through in utero transmission) despite the use of passive/active prophylaxis. For this reason, antiviral treatment in the third trimester can be considered for those women. The choice of antiviral should be restricted to those drugs considered safe in this setting.

Key words: Hepatitis, Macrosomia, Oligohydramnios, Thrombocytopenia

INTRODUCTION

Pregnancy is a physiological phenomenon for most women. During pregnancy, there is a progressive anatomical, physiological, and biochemical change not only confined to the genital organs but also to all the systems of the body. This is principally a phenomenon of maternal adaptation to the increasing demands of the growing fetus. However, pregnancy can be met by various comorbidities and complications, infections being one of them.[1] Six different forms of viral hepatitis have now been defined. Each type of viral hepatitis has its own concerns. The most common viral agents causing hepatitis in pregnancy are hepatitis A virus, hepatitis B virus (HBV), hepatitis C (non-A and non-B hepatitis virus), hepatitis E, hepatitis G, and Epstein-Barr virus. Delta agent hepatitis has also received increasing attention as a cause of hepatitis.

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Viral hepatitis in pregnancy has incited a lot of debate and discussion all throughout the world. Various authors[2,3] have reported findings ranging from no difference in fetal/maternal outcome to nearly universal fatality. Interestingly, these different types of outcome are peculiar to certain geographical areas. For example, there was no increased maternal mortality due to Hepatitis E infection in pregnancy in the reports from South India[4] and Egypt,[5] but a significantly higher rate of mortality has been reported from North India.[6] This is despite the fact that all these geographical areas are endemic for hepatitis E infection.[7] Viral hepatitis is the most common cause of jaundice in pregnancy. Jaundice is defined as a clinical manifestation of hyperbilirubinemia which consists of deposition of bile pigments in the skin, resulting in yellowish staining of the skin and mucous membrane. Normal serum bilirubin level is <1 mg/dl. Clinical jaundice is manifested if serum bilirubin level >2 mg/dl. Jaundice complicates 3–5% of pregnancies and is one of the important causes of maternal and neonatal morbidity and mortality worldwide. It is responsible for 10% of maternal deaths.[8]

Acute hepatitis A is self-limiting disease. Its prognosis in pregnancy is same as that in non-pregnant patient.

Hepatitis B[9]

Hepatitis B is caused by a small DNA virus. The intact virus is termed the Dane particle. Hepatitis B surface antigen (HBsAg) is present on the surface of the virus and also circulates freely in the serum in spherical and filamentous forms. The middle portion of the Dane particle contains hepatitis B core antigen (HBcAg). The core antigen is present in hepatocytes and does not circulate in the serum. Hepatitis B e antigen (HBeAg) is encoded by the same portion of the viral genome that codes for the core antigen. The presence of HBeAg indicates an extremely high viral inoculum and active virus replication. The incubation period of hepatitis B is 6 weeks to 6 months. Hepatitis B is transmitted by parenteral and sexual contact.

Hepatitis C[9]

Hepatitis C virus (HCV) (previously termed non-A and non-B hepatitis) is a single-stranded RNA. The principal risk factor for acquiring HCV is the same as for hepatitis B. Specific tests: it is confirmed by identifying the antibody to HCV. Hepatitis C viral RNA can be detected by polymerase chain reaction assay of serum soon after infection as well as in chronic disease.

Hepatitis D[9]

Hepatitis D requires HBV for replication and expression and so occurs only in people already infected with hepatitis B. In acute hepatitis B, once HBsAg clears the bloodstream, so does hepatitis D. Vertical transmission of hepatitis D virus has been documented. Transmission is uncommon, however, because the measures used to prevent perinatal infection with HBV are almost uniformly effective in preventing infection by hepatitis D.

Hepatitis E[9]

Hepatitis E infection during pregnancy and in the third trimester is associated with more severe infection and might lead to fulminant hepatic failure and maternal death. In outbreaks of waterborne hepatitis E in India and Asia, the case-fatality rate is 1–2% and up to 10–20% in pregnant women. Mortality rates among pregnant women, especially those infected in the third trimester, have ranged between 15% and 25%, much higher that men and non-pregnant women. It has got high incidence of abortion, fetal death, and still birth.[10]

Hepatitis G[9]

Hepatitis G infection is more likely in people already infected with hepatitis B or C or who have a history of intravenous drug use and HIV. Vertical transmission is high and hepatitis G probably does not cause chronic active hepatitis or cirrhosis.

Aims and Objectives

The aim of the study was to study the maternal and fetal outcome in viral hepatitis in pregnancy.

MATERIALS AND METHODS

The study entitled viral hepatitis in pregnancy – Study of its effect on maternal and fetal outcome was a prospective and observational study conducted in the Postgraduate Department of Gynecology and Obstetrics, Lalla Ded Hospital, Government Medical College Srinagar over a period of one and a half year after obtaining clearance from the Institutional Ethical Committee and written informed consent from the patient.

Inclusion Criteria

All pregnant women with positive serology for viral hepatitis at any gestational age and those who are willing to participate were enrolled in the study.

Exclusion Criteria

Patients with chronic liver disease, jaundice with negative serology, HELLP syndrome, acute fatty liver, intra hepatic cholestasis, drug-induced jaundice, pregnancy with hypertension, pregnancy with diabetes, multiple pregnancy, antepartum hemorrhage, and previous cesarean section(s) were excluded from the study.

Methodology

After admission, all patients had a thorough history and clinical examination. The period of gestation was calculated on the basis of last menstrual period and early

Table 1: Various parameters

Patient characteristics	Number	Percentage
Age in years		
25–29	36	53.7
30–34	23	34.3
≥35	8	11.9
Total	67	100
Mean±SD (Range)=30.3±3.64 (26-45)		
Gravidity		
Primigravida	20	29.9
Gravida 2	26	38.8
Gravida 3	13	19.4
≥Gravida 4	8	11.9
Icterus		
Present	10	14.9
Absent	57	85.1
Edema		
Present	8	11.9
Absent	59	88.1
Icterus liver span		
Present	5	7.5
Absent	62	92.5
Status of Liver Function		
Normal	47	70.1
Deranged	20	29.9
Hepatitis Serology		
Hepatitis B	33	49.3
Hepatitis C	32	47.8
Hepatitis A	1	1.5
Hepatitis E	1	1.5
Liver morphology on USG		
Hepatomegaly	4	6.0
Liver atrophy	2	3.0
Normal hepatobiliary system	61	91.0
Gestational age at delivery		
<37 Weeks	12	17.9
≥37 Weeks	55	82.1
Mean±SD=37.2±1.87		
Mode of delivery		
Normal delivery	25	37.3
Cesarean section	42	62.7

Table 2: Indications for cesarean section, maternal, and fetal complications

Patient characteristics	Number	Percentage
Indications for LSCS		
Acute fetal distress	23	54.8
Oligohydramnios	6	14.3
Color Doppler changes	3	7.1
Cephalopelvic disproportion	3	7.1
Non-progression of labor	2	4.8
Intra uterine growth restriction	2	4.8
Macrosomia	2	4.8
Malpresentation	1	2.4
Maternal complications		
Thrombocytopenia	14	33.3
Postpartum hemorrhage	3	7.1
Hypoglycemia	3	7.1
Birth weight (kg)		
<2.5 Kg	7	10.4
2.5–3.5 Kg	58	86.6
>3.5 Kg	2	3.0
Fetal complications		
Low birth weight	7	16.7
NICU admission	16	38.1
Intra-uterine Death	2	4.8

Table 3: Apgar score at 1 and 5 min among study neonates

Apgar score	Number	Percentage
1 Min		
<7	25	37.3
≥7	42	62.7
5 Min		
<7	18	26.9
≥7	49	73.1

ultrasound which ever was available. The blood sample was collected and was sent for biochemical studies for liver function test, coagulation profile, and serological tests for Immunoglobulin (Ig)M anti-HAV, HBs antigen, IgM anti-HEV, and IgM anti-HCV using commercially available ELISA kits. The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar and pie diagrams.

RESULTS

In our study, patient's age in our study ranged between 26 and 45 years with a mean age of 30.3 ± 3.64. Majority of patients age ranged between 25 and 29 years 53.7% (*n* = 36). 26 (38.8%) in our study were gravida 2 followed by 20 (29.9%) primigravida, 13 (19.4%) were gravida 3, and 8 (11.9%) were >gravida 4. Icterus was observed in 10 (14.9%) at presentation. Edema at presentation was observed in 8 (11.9%) patient. Increased liver span was seen in 5 (7.5%) patients. Liver function test was deranged in 20 (29.9%) patients in our study. There were 33 (49.3%) hepatitis B, 32 (47.8%) hepatitis C patients while 1 (1.5%) each had hepatitis A and hepatitis E. On ultrasonography, 61 (91%) patients had normal hepatobiliary system, in 4 (6%) patients findings were suggestive of hepatomegaly while 2 (3%) had liver atrophy. Gestational age at delivery was >37 weeks in majority of patients, that is, 55 (82.1%) while <37 weeks gestation was seen in 12 (17.9%) patients. Majority of women delivered through cesarean section, that is, 42 (62.7%) while normal delivery was seen in 25 (37.3%) patients.

Indications for cesarean section were acute fetal distress in 23 (54.8%) and the other indications included oligohydramnios, color Doppler changes, cephalopelvic disproportion, non-progression of labor, intra uterine growth

restriction, macrosomia, and malpresentation were seen in 6 (14.3%), 3 (7.1%), 3 (7.1%), 2 (4.8%), 2 (4.8%), 2 (4.8%), and 1 (2.4%) women, respectively. Thrombocytopenia was observed in 14 (3.33%) women and postpartum hemorrhage and hypoglycemia in 3 (7.1%) patients each. Normal birth weight was observed in 65 (97%) patients while as 2 (3%) babies were overweight. The mean birth weight was 2.73 ± 1.26 kg. There were 42 (62.7%) patients with 1 min Apgar >7 compared to 49 (73.1%) at 5 min Apgar score >7 days. Fetal outcomes such as NICU admission were observed in 16 (38.1%) NICU admission, low birth weight in 7 (16.7%), and 2 (4.8%) intra-uterine deaths [Tables 1-3].

DISCUSSION

Acute viral hepatitis is the most common form of liver disease worldwide and it frequently affects women of childbearing age, either as an acute infection or as a chronic disease.[11] It is still a major public health concern of developing countries such as India, despite improving socioeconomic condition, sanitation, and health awareness.[12] HEV infection occurring in young adults is a known phenomenon with a predisposition to pregnant women.[13] A total of 67 pregnant females were included in this study with serology positive for viral hepatitis. Patient's age in our study ranged between 26 and 45 years with a mean age of 30.3 ± 3.64. Majority of patients age ranged between 25 and 29 years 53.7% (n = 36). Similar age group was affected (25–29 years) in a study conducted by Chandni *et al*., (2021).[14] Same age group was reported by Jethwa *et al.* (2016)[11] (46%) and by Terrault NA *et al.* (2017)[15] (50.7%) in their respective studies. In our study, 26 (38.8%) patients were gravida 2 followed by 20 (29.9%) primigravida, 13 (19.4%) were gravida 3, and 8 (11.9%) were >gravida 4. Similar reports were reported by Chandni *et al*., (2021).[14] In their study, majority of women were primigravida (40.45%) followed by gravida 2 (35.39%). Elsheikh *et al.* (2007)[16] conducted a study where maximum patients were second gravida.

In our study, most common clinical presentation was icterus. It was noticed in 10 (14.9%), 8 (11.9%) had edema, and 5 (7.5%) had increased liver span. About 100% of patients had icterus at the time of admission (Choudhary *et al*., 2017)[17] similar observations were also confirmed by Prasad *et al*., (2016).[18] In the present study, deranged LFT was observed in 20 (29.9%) patients. Desai *et al*., (2020)[19] did a study in which 29 patients (58%) had SGOT and SGPT < 200 IU/L. Thirteen patients (26%) had SGOT and SGPT between 200 and 500 IU/L. Eight patients (16%) had SGOT and SGPT more than 500 IU/L and all of them were the cases of viral hepatitis. In our study, 33 (49.3%) had hepatitis B, 32 (47.8%) had hepatitis C, and 1 (1.5%) each hepatitis A and hepatitis E. Hepatitis B infection was responsible for maximum cases of viral infection contributing to (106) 92.9% in a study done by Chaitra *et al*., (2019).[20] Similar results was noted in the study conducted by Shukla *et al.* (2011),[21] whereas the study conducted by Jaiswal *et al*., (2001)[22] and Aziz *et al*., (1997)[23] reported the commonest virus to be hepatitis E. On ultrasonography, hepatomegaly was found in 4 (6%) patients and liver atrophy in 2 (3%) patients while majority 61 (91%) had normal hepatobiliary system. Hepatomegaly was also confirmed in 18.96% in a study by Choudhary *et al*., (2017),[17] 20% by Desai *et al*., (2020).[19]

In our study, gestational age at delivery in 55 (82.1%) women was >37 weeks, full-term gestation was also observed by Chandni *et al*., (2021)[14] in 44.9% against pre-term in 55.1% patient. About 52% of women had pre-term delivery and rest 48% had term delivery in a study by Desai *et al*., (2020).[19] Another study by Patil *et al*., (2017),[24] majority of patients were in the third trimester of pregnancy (82%) with mean gestational age at presentation of symptoms that was 34.44 + 6.28 weeks. Out of 67 patients, 42 (62.7%) women delivered through cesarean section in our study while 25 (37.3%) had normal vaginal deliveries. Maternal outcome and complications were analyzed in terms of mode of delivery, 43 (37.7%) patients delivered vaginally, whereas 71 (62.2%) underwent cesarean section in a study by Chaitra *et al*., (2019).[20] Acute in indications for cesarean section women, 42 women include acute fetal distress in 23 (54.8%). Acute fetal distress was observed in 38.3% pregnant women in a study conducted by Yang *et al.* (2002).[25] The main reason was chorion angioipathy induced by hepatitis B infection of placenta. Prasad *et al*., (2016)[18] conducted a study of hepatitis E in pregnancy in which 14% of women underwent LSCS for fetal distress and severe oligohydramnios, oligohydramnios in 6 (14.3%), color Doppler changes and cephalopelvic disproportion in 3 (7.1%) patients each, non-progression of labor, IUGR, and macrosomia in 2 (4.8%) patients while 1 (2.4%) patients had malpresentation. Oligohydramnios was observed in 11.2% of women in a study by Sujatha and Konda (2019).[26] Maternal complications such as thrombocytopenia were observed in 14 (33.3%) and postpartum hemorrhage and hypoglycemia in 3 (7.1%) patients each. Monteith *et al*., (2014)[27] conducted a study in which prevalence of thrombocytopenia was 10.3%. Sujatha and Konda (2019)[26] conducted a study on 93 hepatitis B-positive women in which postpartum hemorrhage was observed in 16.1%. Normal birth weight (2.5–3.5 kg) was seen in 58 (86.6%) newborns, 7 (10.4%) were low birth (<2.5 kg) while 2 (3%) were overweight (>3.5 kg). The mean birth weight was 2.73 ± 1.26 kg. Majority of the LBW cases (16%) were due to prematurity and all of them had NICU admissions (Sujatha A and Konda S, 2019).[26] Low birth weight was also observed in 7.6 and 8.3% by Kumar *et al.* (2004)[6] and Medhat *et al.* (1993),[28] respectively.

There were 42 (62.7%) patients with 1 min Apgar >7 compared to 49 (73.1%) at 5 min Apgar score >7 days. Cui *et al*., (2016)[29] conducted a study in which majority of women (488) had Apgar at 7 min with a mean Apgar score of 9.90 ± 0.53 at 5 min. Fetal outcomes such as NICU admission were observed in 16 (38.1%) NICU admission, low birth weight in 7 (16.7%), and 2 (4.8%) intra-uterine deaths. Chandni *et al*., (2021)[14] conducted a study in which low birth weight (25.33%) formed the bulk of NICU admission (54%) while IUD was seen in 10.11% of women which is similar to the results reported by Jethwa *et al*., (2016)[11] in their study (25% of low birth weight and 33.3% of NICU admission).

CONCLUSION

Identification of HBV-positive pregnant women remains the most effective way to prevent HBV transmission to newborns thanks to a very effective passive/active prophylaxis at birth. However, in the case of women with very high viremia, a non-negligible proportion of newborns can acquire the infection (probably through in utero transmission) despite the use of passive/active prophylaxis. For this reason, antiviral treatment in the third trimester can be considered for those women. The choice of antiviral should be restricted to those drugs considered safe in this setting. Decisions regarding the time of eventual discontinuation should consider the stage and activity of liver disease and of infection, taking into account also the risk of postpartum hepatitis flare. Breastfeeding is not contraindicated for HBV patients. However, it is not recommended for women taking antiviral drugs. Finally, there is no clear evidence that ECS reduces the risk of mother-to-child transmission compared to vaginal delivery. Urgent redressal of issues pertaining to sanitation and provision for clean drinking water for citizens of India is the need of the hour as HEV is fecooral in transmission.

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