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To Study the Fetal and Maternal Outcomes in Pregnancy Associated with Acute Viral Hepatitis

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ABSTRACT
Acute Viral hepatitis in pregnancy is a high risk pregnancy and is a subject of continued interest. There are studies showing results ranging from no difference in maternal and fetal outcome to virtually lethal outcome in the form of fulminant hepatitis and hepatic failure. Each type of viral hepatitis has different implications over the course of pregnancy. To determine the maternal and fetal outcomes and perinatal transmission in pregnancy associated with acute viral hepatitis. 200 mothers with positive viral serology were followed clinically as well as laboratory and radiological investigations throughout the pregnancy. The data were tabulated in Microsoft EXCEL and analysed with SPSS V. 24 software. Associations evaluated with Chi square test. Hepatitis E is the most prevalent and associated with high maternal mortality (94.3%), DIC (92.9%), HE (97.7%), PPH (63.6%), IUD (94.4%), preterm birth (67.4%), low birth weight (83.3%). Hepatitis A was rather associated with anaemia (33.3%), abnormal renal function (23.1%), PPH (27.3%). Precautionary measures if timely taken can reduce the incidence of Hepatitis. At present there is no effective vaccination against Hepatitis E in pregnancy, however proper management of patients with Hepatitis E Virus infection can reduce the burden of disease.

INTRODUCTION

The common cause of jaundice in pregnancy is acute viral hepatitis the other causes being acute fatty liver of pregnancy, obstetrics cholestasis predominantly[1]. From various journals we came to know that maternal and fetal outcomes in acute viral hepatitis can range from no effects to severe adverse effects. We would try to introduce our results. Acute viral hepatitis is broadly classified under five types, Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, Hepatitis E.

Hepatitis A: Virus is a positive-sense, single-stranded RNA virus belonging to the family Picornaviridae[2].

The virus is mostly transmitted through the fecal-oral route. This is most prevalent in developing countries with poor hygiene and sanitation, which results in food and water contamination. The average incubation period for hepatitis A is 30 days. Hepatitis A virus has the highest concentration in the feces, serum, and saliva, respectively. Intrauterine and perinatal transmission of Hepatitis A is a rare occurrence[3,4].

Hepatitis B: Virus (HBV) is an enveloped virus, partially double-stranded virus, circular DNA genome and belonging to the family Hepadnavirus. Chronic hepatitis B infection is associated with cirrhosis and hepatocellular carcinoma. Hepatitis B virus does not cross the placenta but can infect the fetus if there are breaks in the maternal-fetal barrier. Perinatal transmission accounts for more than 50% of cases worldwide. Pregnant women with E antigen (HBeAg) have a 90% likelihood of their new-borns being infected with the hepatitis B virus[5]. Other modes of transmission include sexual intercourse, body fluids, and blood transfusion.

Hepatitis C: Virus (HCV) is a partially double-stranded, plus-sense RNA virus with 11 major genotypes and 15 different subtypes[6]. Hepatitis C is a major cause of cirrhosis and hepatocellular carcinoma worldwide. The major mode of transmission through infected blood transmission, intravenous drug users sharing needles, sexual contact and mother-to-child transmission[7]. Invasive procedures such as amniocentesis and chronic villus sampling break the maternal-fetal barrier and increase the risk of vertical transmission of the hepatitis C.

Hepatitis D: Is caused by the hepatitis delta virus (HDV), a single-stranded, circular RNA and a defective virus with an incomplete RNA requiring the assistance of the Hepatitis B virus, specifically hepatitis B surface antigen (HBsAg), to be infectious[8].

Hepatitis D is mostly transmitted through the same route as the Hepatitis B virus. Coinfection of Hepatitis D virus and Hepatitis B virus leads to severe acute infection.

Hepatitis E: Virus (HEV) is an icosahedral, non-enveloped virus with a single-stranded, positive RNA virus classified into the family Hepeviridae and the genus Orthohepeviurs. There about 7 genotypes of the Hepatitis E virus, and genotypes 1-4 are known to affect humans[9].

The main transmission route for HEV infection is the fecal-oral route and is most prevalent in developing countries with poor sanitation. Sporadic case reported in developed countries are attributed to the Immunocompromised state[10].

MATERIALS AND METHODS

This single centered instituition based prospective observational study was conducted in the indoor patients of gynaecology and obstetrics department of Nil Ratan Sircar Medical College and Hospital from January 2019 to June 2020.All uncomplicated pregnant mother who were admitted with acute viral hepatitis were enlisted. Patients who has existing co morbidities like chronic hypertension, overt diabetes, obstetrics cholestasis, chronic liver disease, or diseases like gilbert syndrome, haemolytic anaemia, hemoglobinopathies and seropositive for HIV 1-2 ,post organ transplantation patients and patients not giving consent for study were excluded. After fulfilling eligibility criteria and giving consent we had taken 200 patients for our study. Amongst the pregnant mothers, women with symptoms of hepatitis like fever, icterus, nausea, vomiting were admitted to find out the cause. A detailed history, clinical examination complete blood count, liver function test coagulation profile ultrasound was done. Patients were counselled for regular follow up and strict hospital delivery. Investigations were repeated as and when required. Maternal and fetal outcomes were analysed in terms of abortions, preterm labor, intrauterine fetal death, DIC, hepatic encephalopathy, PPH, maternal mortality, low birth weight, NICU admission, etc.

Statistical analysis: The data is tabulated in Microsoft excel and analysed with SPSS V.24 software. The categorical are presented with frequency and percentage. Chi square test is used to evaluate the associations. The $p \leq 0.05$ is considered as statistically significant.

RESULTS

Table 1 we infer 59.5% mother were between age 20-30 yeears, most of them were multiparous. Maximum mothers were detected during their second

trimester. Amongst all 59% mothers were affected with hepatitis E, followed by 28% mothers affected with hepatitis A. Around 73.5% mothers delivered vaginally.

Table 2 shows the percentage wise distribution of various parameters with each type of hepatitis.

Table 3 we could see that complications like abnormal liver and renal function test were seen mostly in mothers affected with Hepatitis E (87.5% and 57.7% respectively) Fulminant complications like Hepatic Encephalopathy (97%), DIC (92.9 %), were also seen mostly with hepatitis EPPH was seen associated with hepatitis E (63.6 %) and hepatitis A (27.3%). Hepaitis B and C are not associated with adverse complications.

Table 4 we could infer worst adverse outcomes like are mostly associated with hepatitis E (94.4-67.4% respectively). Preterm birth is also seen with Hepatitis A (19.6 %). Hepatitis E is associated with high maternal mortality. 83.3% of low birth weight babies were attributed to Hepatits E.

Table1. Distribution of general parameters

Parameters	No. (%)
Maternal age	
<20 years	21 (10.5)
20-30 years	119 (59.5)
>30 years	60 (30.0)
Parity	
Primi	84 (42.0)
Multi	116 (58.0)
Gestational age	
1st trimester	9 (4.5)
2nd trimester	101(50.5)
3rd trimester	90 (45%)
Subtypes of hepatitis	
A	56 (28.0)
B	11 (5.5)
C	15 (7.5)
E	118 (59.0)
Mode of delivery	
Vaginal	147 (73.5)
LSCS	53 (26.5)

DISCUSSIONS

In our study, we found maximum affected mothers were multigravida (58.0%) and were in the age group 21-30 years (59.5%), mostly belonging to second trimester (52.0%).We also found that ,56 (28.0%) mothers were diagnosed with hepatitis A, 11 (5.5%) mothers with hepatitis B, 15 (7.5%) mother with hepatitis C and 118 (59.0%) mothers with hepatitis E. Most of them underwent vaginal delivery (73.5%). We found 16 mothers with severely raised bilirubin and liver enzymes and 26 mothers with abnormal renal function. Most of them were affected with hepatitis E. In our study, total 44 mothers developed Hepatic encephalopathy and 70 mothers developed DIC, of which 97.7-92.9% were affected with Hepatitis E respectively. Of the 11 mothers who developed PPH, 63.6% were affected with Hepatitis E, 27.3% were affected with hepatitis A. We found that total there were 18 miscarriages and 18 intrauterine foetal death of which 94.4% each were associated with Hepatitis E. There were total 46 preterm birth, 67.4% were affected with Hepatitis E, 19.6% with Hepatitis A. We found total 166 live births, of which 44 babies required NICU admission and 3 babies underwent neonatal death and all the 3 mothers were affected with Hepatitis E. There were total 35 maternal death, 94.3% were associated with Hepatitis E, 5.7% were associated with Hepatitis A. We found total 60 low birth weight babies.

Javed *et al*.[11] found that incidence of HEV in pregnant mother was 15%, with 14.2% occurance of preterm labour, 19% intra uterine fetal death, 4.4%

Table 2: Percentage (%) wise distribution of hepatitis with various parameters

Hep	Anaemia	GDM	Oligo	ARF	HE	DIC	Abortions	Preterm	IUD	Live birth	Maternal mortality	PPH	LBW	NICU
A	12.5	19.6	1.7	10.7	-	8.9	1.7	16	1.7	98.2	3.5	5.3	14.2	25
B	-	9	18.18	-	9	-	-	27.2	-	100	-	-	9	36
C	33	33	13.3	33	-	-	-	20	-	100	-	6.6	6.6	26
E	7.6	19.4	11	12.7	36	55	14.4	26.2	14.4	72	27.96	5.9	42.6	18.6

Table 3: Association of various parameters with different subtypes of hepatitis

	Subtypes of hepatitis						
Parameter	A	B	C	E	Total	Chi square value	p-value
Bilirubin>10 mg dL^{-1}	2 (12.5%)	0 (0.0%)	0 (0.0%)	14 (87.5%)	16 (100.0%)	6.147	0.105
Liver enzymes>5 times the upper limit	2 (12.5%)	0 (0.0%)	0 (0.0%)	14 (87.5%)	16 (100.0%)	6.147	0.105
Abnormal renal function	6 (23.1%)	0 (0.0%)	5 (19.2%)	15 (57.7%)	26 (100.0%)	7.394	0.06
HE	0 (0.0%)	1 (2.3%)	0 (0.0%)	43 (97.7%)	44 (100.0%)	35.434	0.000*
DIC	5 (7.1%)	0 (0.0%)	0 (0.0%)	65 (92.9%)	70 (100.0%)	51.655	0.000*
PPH	3 (27.3%)	0 (0.0%)	1 (9.1%)	7 (63.6%)	11 (100.0%)	0.724	0.868

Table 4: Association of maternal and fetal outcomes with different subtypes of hepatitis

	Subtypes of hepatitis						
0	A	B	C	E	Total	Chi square value	p-value
Abortion	1 (5.6%)	0 (0.0%)	0 (0.0%)	17 (94.4%)	18 (100.0%)	10.342	0.016*
Preterm	9 (19.6%)	3 (6.5%)	3 (6.5%)	31 (67.4%)	46 (100.0%)	2.421	0.490
IUD	1 (5.6%)	0 (0.0%)	0 (0.0%)	17 (94.4%)	18 (100.0%)	10.342	0.016*
Live birth	55 (33.1%)	11 (6.6%)	15 (9.0%)	85 (51.2%)	166 (100.0%)	24.569	0.000*
Maternal mortality	2 (5.7%)	0 (0.0%)	0 (0.0%)	33 (94.3%)	35 (100.0%)	21.993	0.000*
LBW	8 (13.3%)	1 (1.7%)	1 (1.7%)	50 (83.3%	60 (100.0%)	21.366	0.000*
NICU admission	14 (31.8%)	4 (9.1%)	4 (9.1%)	22 (50.0%)	44 (100.0%)	2.581	0.461

incidence of abortions, with a case fatality rate of 14.2%. Changede *et al*.[12] found the incidence rate of HEV in pregnant mother was 42%, occuance of intrauterine death was 37%, case fatality rate of 40% incidence of DIC coaghlopathy being 65%. In our study we found, incidence of HEV as 59%, occurance of abortions and preterm labor as 14.4% and 26.2% respectively. We found incidence of intrauterine fetal death was 14.4%, case fatality rate was 27.9%, incidence of coagulopathy was 55%. Our live birth rate was 72%.

Eran elinav *et al* found the incidence of HAV in pregnancy was 13 %, with occurance of preterm labour being 30-15% low birth weight. Ho Seong *et al* found that the incidence of of HAV in pregnancy is 12-8.3% mothers had premature labour and abortions respectively. From our study, we found that the incidence of HAV in pregnancy 56-7% had premature labor. 25% of neonates were admitted in NICU.

CONCLUSION

After this statistical analysis, we come to a conclusion that acute viral hepatitis has variable outcomes in pregnancy. The most common subtype of acute viral hepatitis is hepatitis E followed by hepatitis A. Hepatitis E is associated with adverse maternal outcomes like altered renal function, hepatic encephalopathy, disseminated intravascular coagulation, post-partum haemorrhage and maternal mortality .It is also associated with abortions, preterm birth, intrauterine fetal death, low birth weight of neonates. Hepatitis A is found to be associated with abnormal renal function, disseminated intravascular coagulation, post-partum haemorrhage. It is also associated with preterm birth, low birth weight of neonates. Hepatitis B and C are not significantly associated with adverse maternal and fetal outcomes.

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