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Fetomaternal Outcome in Pregnancy with Hepatitis E Infection

By Dr. Sampada

Abstract- *Background:* HEV infection, a major public health concern, is known to cause large-scale epidemic and sporadic cases of acute viral hepatitis in developing countries. The infection occurs primarily in young adults and is generally mild and self-limiting; however, the case fatality rate is reportedly higher among pregnant women.

Methods: Our study, a retrospective observational study, was conducted in a tertiary care centre for over a period of 3 years (Jan 2017 to Jan 2020) to find out the fetal and maternal outcome in pregnant women with HEV infection.

Results: A total of 38antenatal cases with Anti-HEV IgM-positive were included, and the maternal-fetal outcome was analyzed. The maternal mortality was 52.63% especially during 3rd trimester and post-partum period, including 5 antenatal death. The most common maternal complication was acute fulminant hepatitis (39.5 %), DIC (36.8 %) and hepatic encephalopathy (31.6%). Prematurity (33.3% of total live births) and Still births (32.3 %) including4fresh still births were the commonest fetal complications noted.

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Conclusion: Our study shows that pregnant woman with acute viral hepatitis due to hepatitis E virus infection had a high mortality rate especially during 3rd trimester and post-partum period with poor obstetric and fetal outcome.

Keywords: Hepatitis E, pregnancy, fulminant hepatic failure, maternal mortality, still births, hepatic encephalopathy, coagulopathy.

I. Introduction

Hepatitis E virus is a major cause of hepatitis and death in developing world and disproportionate cause of deaths among pregnant women[1].It is a non-enveloped, single-stranded RNA virus and is only virus within the genus Hepevirus and family hepaviridae[2]. HEV infectionis primarily transmitted through the feco-oral route[3]. The infection primarily occurs in young adults and is generally mild and self-limiting; however, the mortality rate is higher among pregnant women.[4] The nutritional, immunological and genetic factors play role in pathophysiology of fulminant HEV during pregnancy in developing countries[5]. Diminished cellular immunity (lowered CD4/CD8 cell ratio) and a high level of steroid hormones that influence viral replication during pregnancy appear to be the plausible reasons for severity of the disease[6].

The incidence and severity during pregnancy vary widely around the world. The case fatality rate is 1–2 % in outbreaks of waterborne Hepatitis E in India and Asia, which increases up to 10–20 % in pregnant women[7]. Reason for the difference in the outcome of HEV in different geographical areas remains unclear[8] but could be due to early childhood HEV exposures, producing long-lasting immunity and/or modifying subsequent responses to exposure to the virus. HEV is known to have five genotypes, four of which have been detected in humans; genotypes 1 and 2 are more virulent, genotypes 3 and 4 are more attenuated and accountable for subclinical infections[9].

This disease presents a challenging situation to the obstetrician because of the complications such as postpartum haemorrhage (PPH), preterm labour, preterm premature rupture of membrane (PPROM), maternal coagulopathy, acute fulminant liver failure, spontaneous abortion and intrauterine fetal death (IUFD).

II. Methods & Materials

A retrospective observational study was conducted at a tertiary care centre for over a period of 3 years (Jan 2017 to Jan 2020) to analyse the fetal and maternal outcome in all antenatal patients with Anti-HEV IgM-positive.

Inclusion criteria:

1. All antenatal patients with Anti-HEV IgM-positive.

Exclusion criteria:

2. Patients with Anti-HEV IgM-positive who lost follow up.

III. Observations

Age and parity distribution

Age	Parity		Gestational Age		
	primi	Multi	1st tri	2nd tri	3rd tri
20-25	10	12	-	7	15
26-30	4	10	-	6	8
30-40	1	1	-	-	2

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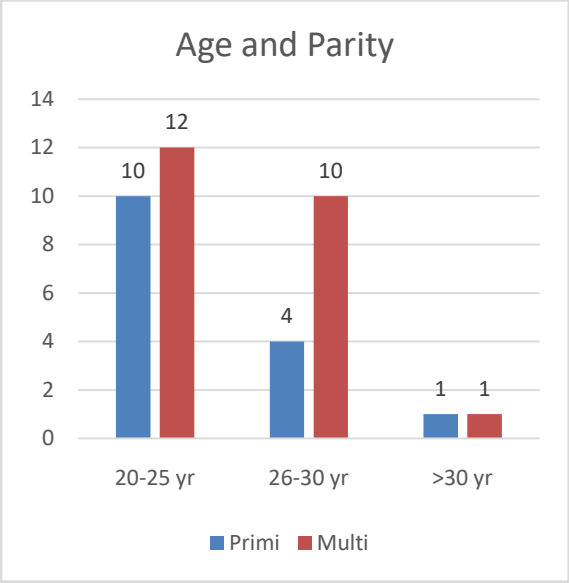
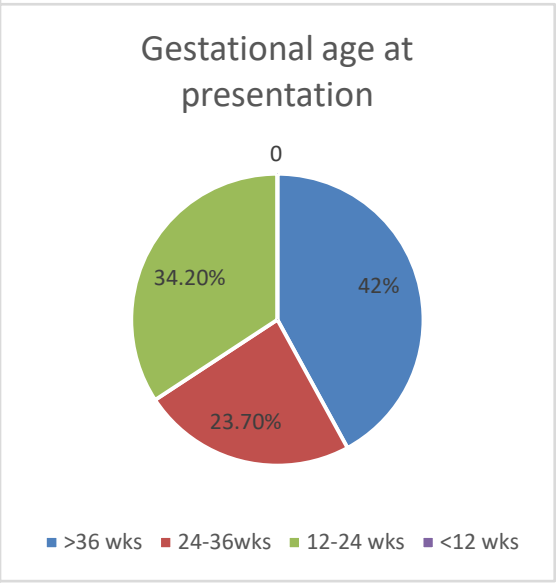




57.9 % belong to the age group 20-25 years followed by 36.8 % belong to 26-30 years and the minimum 5.3% belong to >30 years.

In our study maximum patients belong to third trimester, 42 % presented at > 36 weeks of gestation and 23.7 % between 24-36 weeks and 34.2 % in 12-24 weeks. No patient was found in the first trimester.

Lab parameters	Highest	Lowest	Median	Mean
Hb	13.8	4.6	-	9.09
Total leucocyte count	54000	2500	-	19680
Platelet	5.57 lac	21000	-	1.81 lac
Bilirubin	28	0.5	18.7	25.7
SGOT	4406	29	-	713
SGPT	3491	14	-	507
Prothrombin Time	70	11.3	39.3	27.48
INR	8.78	0.79	2.12	2.68
Creatinine	-	4.4	-	-

Presenting complaint

Most common presenting complaint was yellow discoloration of sclera and dark coloured urine, seen in 89 % cases followed by fever and then nausea, vomiting, altered sensorium.

Fever	9
Nausea, vomiting	6
Lethargy	2
Loss of consciousness	2
Altered sensorium	6
Pruritus	4
Convulsions	1
Jaundice	34
Breathlessness	2
Obstetrics reasons(PROM, PT labour, decreased fetal movement)	4+5+2

Some degree of anemia was seen in 74 % cases.

Total cases with Anaemia	Mild(8-10.9)	Moderate(5-7.9)	Severe(<5)
28 (74 %)	10	16	2

Associated thrombocytopenia (platelet count ranging between 21000 to 101000) was seen among 13 (34 %) patients with 4 having severe thrombocytopenia (< 50000).

IV. Data and Statistical Analysis

Computer based data analysis was done. Data entry sheet was designed and statistical analyses were

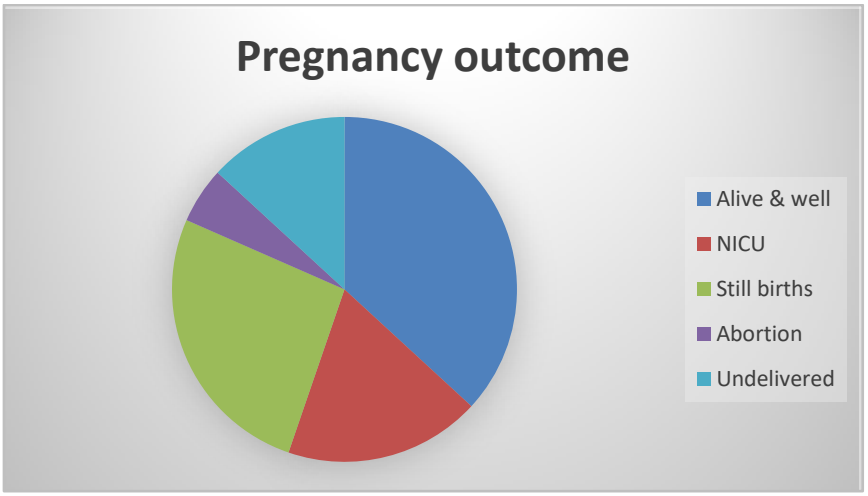
performed by using statistical package for the social sciences software version 16.0 (Chicago IL, USA). Variables considered are age, gestational age at presentation, parity, fetal and maternal outcome.

Quantitative variables e.g. age, gestational age, laboratory parameters were analysed using simple descriptive statistics like mean, median. Qualitative variables e.g. fetal and maternal outcome were calculated using frequency and percentage.

V. Results

a) Pregnancy outcome

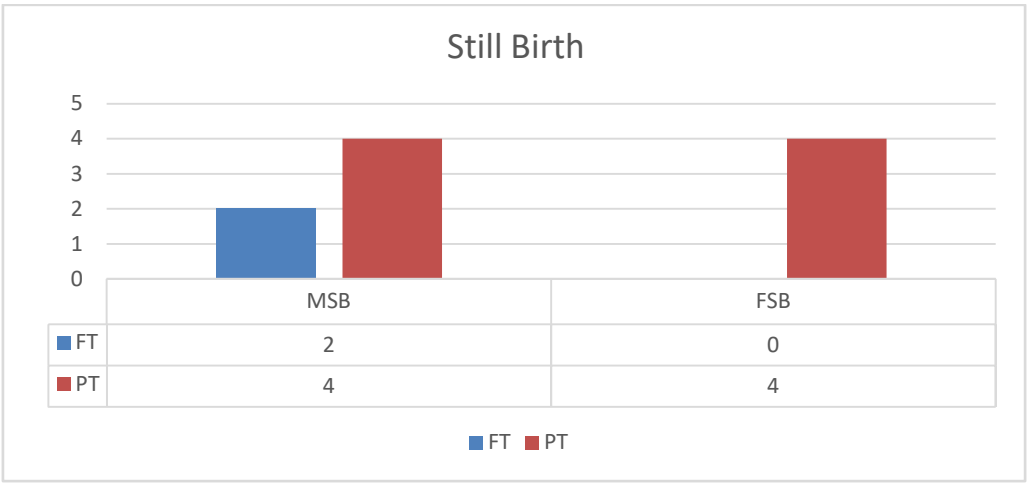
Alive & well	14 (45.16%)
NICU	07 (22.58%)
Still births	10 (32.25%)
Total delivered	31 (100%)
Undelivered	5/38 (13.15%)
Abortion	2/38 (5.26 %)



1. 76 % had low birth weight including 2 very low birth weight.

Total live birth	>/=2.5kg	>1.5kg to <2.5kg(LBW)	</=1.5KG(VLBW)	<1KG(ELBW)
21	5	14	2	0

2. 33% of total live borns were admitted to NICU, reasons being prematurity, very low birth weight and respiratory distress.
3. Still birth rate was 32.4% including 4 fresh still birth.



4. 1 patient had spontaneous abortion at 18 weeks and 1 patient underwent emergency check curettage in view of missed abortion at 16weeks.

b) Mode of delivery

Induction of labour was done in 14 cases by intracervical foleys catheter insertion. Reason for IOL were IUFD, PROM, patients with acute fulminant hepatitis with 37 completed weeks of gestation.

Most of the patients delivered vaginally 25/38 i.e 65.8%. 1 patient required instruemental delivery due to maternal exhaustion in 2nd stage of labour.

There were 6 patients who required lower segment c- section which makes 15.8 %. The indication were meconium stained liquor -1, previous LSCS with PROM -1, previous 2 lscs with ovarian mass-1, severe oligohydramnios -2, previous LSCS with breech -1. 1 patient who underwent LSCS died. 1 patient required exploratory laparotomy for drainage of pelvic haematoma and required blood and fresh frozen plasma. 2 patient who underwent LSCS were transfused blood and fresh frozen plasma both pre and post-operatively .

5/38 patients died in antenatal period and 2/38 had 2nd trimester abortion.

c) Maternal outcome

Mortality	20 (52.63 %)
Intensive care	26 (68.4%)
Blood & blood product transfusion	23 (60 %)

Maternal complications

Hepatic encephalopathy	12(31.6%)
DIC	14(36.8%)
Sepsis	11(28.9%)
PPH	7 (18.4%)
AKI	6(15.8%)
Acute fulminant hepatitis	15(39.5%)
Ascites	3
Hepato-renal syndrome	1
Pleural Effusion	1
Pelvic Hematoma	1

In our study, maternal mortality rate was 52.63 % including 5 antenatal deaths. Most of these patients (75 % i.e 15 out of 20 deaths) presented with acute fulminant hepatitis with hepatic encephalopathy.

Highest bilirubin level observed was 28. Median bilirubin value was 18.7.

Bilirubin level was ranging between 8.7 to 28 with grossly elevated liver transaminases (highest being SGOT- 4406, SGPT- 3491) among the expired patients.

The most common maternal complication was acute fulminant hepatitis (39.5 %) , DIC (36.8 %) and hepatic encephalopathy (31.6%).

Cases complicated by DIC were found to have Prothrombin time ranging between 16.5 to 70, with median value as 39.3. Thrombocytopenia was also seen in association in 92.8 % patients with DIC.

Post partum haemorrhage (18.4 %) and Acute kidney injury (15.8 %) were the other complications which added to mortality and morbidity.

Most of the cases of PPH were managed medically and blood & blood products transfusion. Only 1 case required exploratory laparotomy with devascularisation of uterus.

68 % cases required blood and blood products transfusion reasons being post partum haemorrhage, anemia, disseminated intravascular coagulation.

90 % cases who died were referred from peripheral hospitals with hyperbilirubinemia, hepatic encephalopathy, acute fulminant hepatitis and DIC.

2 cases referred from peripheral hospital with acute fulminant hepatitis with hepatic encephalopathy with coagulopathy died within 6 hours of admission.

VI. Comparative Study

	Maternal mortality	Hepatic Encephalopathy	Acute fulminant hepatitis	DIC
Our study	52.63 %	31.6 %	39.5 %	36.8 %
Yadav S et al[10]	52 %	34 %	38 %	56 %
Prasad GS et al[11]	5 %	9.09 %	9.09 %	32.7%
Singh S et al[12]	65%	-	70%	-

	NICU	Still birth	Abortion
Our study	22.58 %	32.25 %	5.26 %
Yadav S et al[10]	33.34 %	27.78 %	12 %
Prasad GS et al[11]	40.42 %	4.08 %	1.81 %

VII. Conclusion and Recommendation

Our study shows that pregnant women with acute viral hepatitis due to hepatitis E had a high mortality rate especially when infected in 3rd trimester and post-partum period. They also had poor obstetrics and fetal outcome.

Early diagnosis and active management can improve the outcome. Pregnant women should be closely monitored for fetal well-being and signs of fetal distress by periodic ante-natal scan, biophysical profile , non-stress test. They should be counselled about daily fetal kick count.

Hepatitis E is a preventable disease so emphasis should be on sanitation, personal hygiene, hand washing, proper sewage disposal, facilities for clean drinking water and awareness regarding these.

Vaccine against hep- E is available and can reduce the morbidity and mortality associated with pregnancy[12]. HEV 239 vaccine is safe for both mother and fetus and there was no hepatitis E infection in immunised pregnant women[13]. India being an endemic area for hepatitis E with high mortality rate this may be considered as an option.

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Special cases:

1.21 year old, primigravida, with 34 weeks of gestation in a known case of rheumatic heart disease s/p MVR, with c/o fever with chills, jaundice, altered sensorium and moderate anemia referred from periphery.

On admission –

Bili-13.8 SGOT-821 SGPT-219 Hb-8.3 TLC-19600 PLT-61000

Patient was diagnosed to be anti-HEV- IgM positive with hepatic encephalopathy with dengue haemorrhagic fever.

Patient had PPH, developed AKI and died on Day 6 post-natal day.

2.25 year old, G3P2L2 with previous 2 LSCS with 35 weeks of gestation with right ovarian cyst was referred in view of threatened preterm and jaundice.

On admission

Bili-2.6 SGOT-48 SGPT-26, Tumor markers-negative, Viral markers - anti-HEV- IgM positive

USG abdomen s/o right adnexal solid cystic mass (15x10x15cm) likely to be mucinous cystadenoma.

Elective LSCS with right ovarian cystectomy with right salpingoopherectomy with left tubal ligation was done at 37 completed weeks.

Histopathological report was s/o right mucinous cystadenoma.

Patient was discharged with Bili- 0.6 SGOT- 12 SGPT-25

3.38 year old, G2P1L1 with previous LSCS with 32 weeks of gestation with PROM with breech presentation with hyperbilirubinemia was referred from periphery.

On admission,

Bili-13.5 SGOT-289 SGPT-336 PT/INR-WNL Viral markers-anti-HEV- IgM positive.

Emergency LSCS was done, baby was admitted in NICU in view of respiratory distress.

Day 2, post-op patient developed breathlessness and increase in abdominal girth was seen.

USG abdomen was s/o haematoma (450-500 cc) which was drained by pig tail catheter.

2 units PCV and 4 units FFP were transfused.

Patient had 2 episodes of focal seizures, anti-convulsants started.

Patient developed ascitis and pleural effusion.

Emergency exploratory laparotomy was done with drainage of pelvic haematoma.

2 units WB and 4 units FFP were transfused.

Patient was discharged with Bili- 3.2 SGOT-85 SGPT-109