



RESEARCH ARTICLE

A PROSPECTIVE STUDY OF HEPATITIS-E INFECTION AND IT'S FOETAL AND MATERNAL OUTCOME IN PREGNANCY IN MEWAR REGION OF RAJASTHAN

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ABSTRACT

**Aim:** Hepatitis E. viruses (HEVs) are single stranded RNA viruses that cause large epidemics of acute viral hepatitis especially in developing countries and cause adverse maternal and foetal outcome. It affects males and females, both pregnant and non-pregnant. However, in pregnant females HEV infection is more severe often leading to fulminant hepatic failure (FHF) and death.

**Methods:** This study is a prospective study conducted at Pannadhahi Mahila Chikitsalaya, R.N.T. Medical College, Udaipur over a period of 3 years from January 2015 to December 2017 to find out the maternal and foetal outcome in HEV infected pregnant females.

**Results:** A total of 60 symptomatic anti- HEV IgM positive patients were included in this study and their maternal and foetal outcomes were assessed. The maternal mortality was higher as compared to mortality due to other types of hepatitis. The mortality was 11.6%. Prematurity was 70%, IUD 15% and early neonatal deaths were 6.66%.

**Conclusion:** The aim of the study is to make aware the tribal population about the diseases and to increase awareness of proper sanitation, food hygiene and safe drinking water. Variation in maternal morbidity and mortality between different studies need to subtype the viral genotype according to its virulence.

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INTRODUCTION

Hepatitis E earlier known as non-A non-B hepatitis. HEV is enterically transmitted single stranded RNA viruses that causes large scale epidemic and sporadic cases of acute viral hepatitis in developing countries primarily in India, Asia, Africa, and Central America. This agent with epidemiological features resembling those of hepatitis A is a 27 to 34 nm non-enveloped HAV like viruses with a 2700 nucleotide, single strand positive sense RNA genome. HEV infection is a major health problem and is primarily transmitted through faeco-oral route. The incubation period ranges from 3 to 8 weeks (Khuroo, 1997). The infection primarily occurs in young adults and is usually mild and self-limiting however the mortality rate is higher in women especially in pregnant females in second and third trimester (Purcell, 2008; Aggarwal, 2007). The incidence and severity during pregnancy vary widely, in developed countries the incidence is very low 1 in 20,000 whereas in outbreaks of water borne hepatitis in India case fertility rate is 1-2% and up to 10-20% in pregnant females.

Reason for the differences in the outcome of HEV in different geographical areas remain unclear. HEV is known to have 5 genotypes, 4 of which have been detected in humans, genotype 1, 2 are more virulent whereas 3 and 4 are accountable for subclinical infection (Kasper et al., 2015). HEV infection presents a challenge to obstetricians because of complications such as antepartum haemorrhage, preterm premature rupture of membranes, maternal coagulopathy, postpartum haemorrhage & IUFD (Gauri Sayiprasad, 2016). This study was conducted in Pannadhahi Mahila hospital jointly with department of Medicine, R.N.T. Medical College, Udaipur to find the outcome in mother and foetus in a series of HEV infected pregnant females.

MATERIALS AND METHODS

For this a prospective observational study was conducted at the PDMC hospital & dept. of medicine, M.B. Govt. Hospital. R. N. T. Medical College, Udaipur over a period of 3 years. All pregnant females presenting at any gestational age with symptoms like icterus were admitted and were analysed systematically for hepatitis virus' infection e.g.

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Liver function tests and serological analysis. In this study anti-HEV IgM positive pregnant females were included. Patients with clinical evidence of Jaundice due to other causes i.e. HELLP syndrome, acute fatty liver of pregnancy, biliary tract disorder etc. were excluded. Maternal factors such as gestational age at the time of first detection of infection, socioeconomic status, parity, clinical progression of diseases, worsening of symptoms, and mode of delivery, laboratory parameters, foetal and maternal outcome were recorded. The patients were observed for viral hepatitis symptoms and signs, such as fever, jaundice, ascites, peripheral oedema, gastrointestinal symptoms, organomegaly, haemorrhage, paralytic ileus, level of consciousness and altered sensorium. Foetal wellbeing was monitored by ultrasonography and cardio topography(CTG). All routine investigation were also get done. All patients were managed by team of obstetrician, physician and paediatrician. Patients with fulminant hepatic failure were managed in ICU. Treatment given included antibiotics, parental nutrition, ventilatory support and patients with anaemia and deranged coagulation profile were transfused blood and blood products as required. The decision for termination of pregnancy was taken on individualised basis. Labour was monitored according to protocol. All delivered babies were attended by paediatrician and appropriate care and treatment was given. In accordance with the Institutional Ethical Committee norms, this study did not require a documented informed consent of the patients as it did not involve any level of intervention and a standard treatment protocol was followed for all.

## RESULTS

### Demographic and obstetric characteristics

#### This study shows the following results

Data from all the patients who were included in this study was collected. The maximum patients at the time of admission in hospital with hepatitis E infection were 18-25 years of age (78%). Maximum patients were primipara 63.3%. The majority of them were illiterate housewives belonging to poor socio-economic status from rural areas nearby Udaipur. 10% patients presents with symptoms of viral hepatitis in second trimester and 90% in third trimester. The mean gestational age at the presentation of symptoms of hepatitis was 33.6  $\pm$  3.47 SD weeks.

#### Distribution of cases according to age and Gravidity

Age (yrs)	Gravida			%	Total (n=60)
	G1	G2	G3 or more		
18-25	32	10	5	78%	47
26-30	5	2	3	16.66%	10
31-40	1	-	2	5%	3
Total	38	12	10		60

#### Investigation parameters

Mean haemoglobin level gm%	6.8 gm%
Mean leucocyte count [cells x 10 <sup>9</sup> /l]	12 x 10 <sup>9</sup> cells/l
Mean platelet count [cells x 10 <sup>9</sup> /l]	350
Mean serum bilirubin level [mg/dl]	7.6
Mean SGPT [IU/L]	560 IU/L
Median international normalised ratio range	1.8
Mean serum albumin level g/dl]	3.4

### Patients Characteristics

Trimester		
Second	6	10%
Third	54	90%
Area of residence		
Rural	56	93.3%
Urban	4	6.66%

### Obstetric complications and intervention

PROM	9/60	15%
Second trimester		
Second trimester	3/6	50%
Third trimester	6/54	11.11%
Preterm Labour		
Second trimester	42/60	70%
Third trimester	3/6	50%
IUFD		
Second trimester	39/54	72.22%
Third trimester	9/60	15%
PPH		
Second trimester	2/6	33.33%
Third trimester	7/54	12.96%
Coagulopathy		
Second trimester	7/60	11.66%
Third trimester	1/6	16.66%
Blood and blood product transfusion		
Second trimester	6/54	11.11%
Third trimester	8/60	13.33%
Mode of delivery		
Second trimester	1/6	16.66%
Third trimester	7/54	12.96%
Blood-blood products transfusion		
Second trimester	26/60	43.33%
Third trimester	2/6	33.33%
LSCS		
Second trimester	24/54	44.44%
Third trimester	60/60	
Maternal complications and mortality		
Second trimester	50/60	83.33%
Third trimester	6/6	100%
Hepatic encephalopathy with fulminant hepatic failure		
Second trimester	44/54	81.48%
Third trimester	10/54	18.51%
Renal failure		
Second trimester	-	0%
Third trimester	10/54	18.51%
Coagulation defects		
Second trimester	9/60	15%
Third trimester	25/60	41.66%
Blood-blood products transfusion		
Second trimester	7/60	11.66%
Third trimester	9/60	15%
Gastrointestinal haemorrhage		
Second trimester	9/60	15%
Third trimester	25/60	41.66%
Maternal mortality		
Second trimester	7/60	11.66%
Third trimester	7/60	11.66%

### Fatal outcome

IUFD	9/60	15%
Pre-term babies	42/51	82.35%
Still birth	3/51	5.8%
Live birth	48/51	94.1%
Neonatal death	4/51	7.84%
Low birth weight babies	35/51	68.62%
Meconium stained liquor	7/51	13.72%
NICU admission	23/51	45.09%

### Investigation reports

Haemoglobin of maximum patient ranges between 5 to 9 g% with a mean of 6.8 g %. The median leucocyte count was 12 x 10<sup>9</sup> cells/L. Platelet ranged between 2.5 and 4.5 lakhs with a mean of 3.5 lakhs. Prothrombin time was ranged between 13 to 53 seconds with a median of 19 seconds. INR was observed to be 1.8. Serum bilirubin of these patients varied from 1.2 to 22.2mg/dl with a mean of 7.6 mg/dl, SGPT ranged between 60 and 3500 IU/L.

### Obstetric outcome

Antenatal complications- Preterm labour was seen in 42 (70%) and premature rupture of membrane (PROM) was reported in 9 patients (15%). Out of the 60 patients 45 had spontaneous

onset of labour, 5 were induced and 10 patients underwent emergency LSCS (18.5%). The indication for induction was severe oligohydroamnios and foetal distress.

### Complications and mortality

Complications frequently encountered were coagulation disorders (13.33%), renal failure (21.66%), and postpartum haemorrhage (11.66%). Around 25% of patients require intensive care and 43.3% patients required blood and blood product transfusions. There were 7 maternal deaths (11.66%). All had fulminant hepatic failure leading to encephalopathy and multi organ failure.

### Foetal outcome

Forty eight women of hepatitis E were delivered as live babies. Perinatal outcome was considered only after 28 weeks. There were nine intrauterine foetal deaths, three were stillborn and four neonatal deaths. Prematurity was 82% and PROM (15%), out of live birth babies born 68.6% were low birth weight and there were four neonatal deaths. Babies were followed by paediatrician.

## DISCUSSION

Hepatitis E viral infection affects both males and females. In pregnant females (Krawczynski, 2000) it causes severe fulminant hepatitis and is responsible for very high maternal and foetal morbidity and mortality. The exact mechanisms of this still remains to be explained. Compared to other studies of hepatitis E in pregnancy the females of our study are young (Kumar *et al.*, 2004; Tahira *et al.*, 2013). Manifestations are more severe in primigravida as compared to multigravida. Most of the subjects of this study belongs to lower socio-economic status and rural tribes. (Mewar region is mainly a tribal zone). The present study shows lower mean haemoglobin, lower mean serum albumin, and INR, Prothrombin time as compared to other studies (Kumar, 2004; Tahira *et al.*, 2013; Khuroo *et al.*, 2006). With respect to the severity of liver failure, the present study shows 15% cases of fulminant hepatic failure with two women in second trimester and seven in third trimester.

Kumar *et al.* (2004) have reported 33% of incidence rate of FHF in a small study of 28 patients. There was also difference in the number of cases of FHF with some other studies. The reason for differences in FHF in different geographical areas is unknown but it may be due to early childhood exposure or maybe due to virulence of different genotypes of Hepatitis E viruses. This virulence ability of genotypes might play a role in determining the viral subtype which is common in pregnancy. Obstetric complications in present study included preterm labour 42/60 (70%), PROM 9/60 (15%), postpartum haemorrhage 7/60 (11.66%). There were 10 cesarean sections done for various obstetrical complications such as abruptio-placentae, transverse lie, placenta previa, previous LSCS and foetal distress. Subtotal hysterectomy of three was done, out of which 2 were done during cesarean section for placenta previa and atonic PPH and third one was done six hours after cesarean section due to uncontrollable atonic postpartum haemorrhage. Patient was reopened and subtotal hysterectomy with internal iliac ligation by cardiovascular surgeon was done. Out of these three patients two died on post-operative day 5 and 8 due to DIC, hepatic encephalopathy and renal failure.

Induction of labour was performed for non-reactive NST and oligohydroamnios. In this study we observed that prognosis is better when labour occurs spontaneously (Khuroo, 1997; Kasper *et al.*, 2015). Maternal mortality was seen in 7 patients. All of them presented with fulminating hepatic failure. Maternal mortality was 11% in our study as compared to other studies. MMR in a study from Pakistan and other studies from North India vary from 15 to 41% (Kumar, 2004; Tahira, 2013; Asha Ranjan, 2017). As regards to foetal outcome low birth weight babies formed the bulk 35/51 (68.62%) and NICU admission were 23/51 (45%). All the patients with fulminant hepatic failure had poor foetal outcome, seven intrauterine foetal death (IUID) and two neonatal deaths. Various studies show that there is severe maternal outcome in patients with IUID. Same was observed in our study where all the nine patients who were present with IUID had severe diseases for example coagulopathy, renal failure, seven of them died subsequently.

### Conclusion

HEV infection is a major health problem and has more morbidity and mortality among pregnant females. HEV has more complication rates and poor foetal outcomes among pregnant patients. In present studies most of the affected females were of lower socio-economic status and resided in tribal areas, this could form the basis for sponsored vaccination programmes in endemic areas and susceptible population and make the population of endemic areas aware of safe drinking water and food hygiene.

### Compliance with ethical standards

**Conflict of interest:** The authors declare that they have no conflicts of interest.

**Ethical approval:** Not required.

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