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Original Research Article

Study of feto-maternal outcome in patients with hepatitis E infection during pregnancy

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ABSTRACT

Background: Hepatitis E is considered as a common cause of high maternal morbidity and mortality particularly in third trimester and also high perinatal morbidity and mortality. Thus, this study is conducted to evaluate the feto-maternal outcome in patients infected with hepatitis E during pregnancy.
Methods: It is a retrospective observational study conducted in department of obstetrics and gynecology at L. G. hospital. Fifty pregnant women with clinical hepatitis in third trimester of pregnancy were included in this study and thorough investigation were carried out. Patients were monitored till postpartum period and fetal monitoring data were collected from neonatal ICU.
Results: In this study, majority of pregnant patients with hepatitis B were admitted during monsoon season suggests that HEV outbreaks are more common during monsoon months. Majority of the patients (70%) were emergency cases. Majority of these patients (82%) were belonged to lower socio-economic class. Co-infection with HAV was in 2% and with HBV in 4%. S. bilirubin >15 mg/dl in 16% of patients. PT and APTT were raised in 28% of patients. FDP was raised in 70% of patients. 76% were delivered vaginally and 22% were delivered by LSCS. Most common complication in HEV infected pregnant women was disseminated intravascular coagulation (DIC) (26%). Maternal mortality rate is 14%. Out of 50 patients, 88% delivered live baby, out of which 72% needed NICU admission. Perinatal mortality rate was as high as 28%.
Conclusions: Hepatitis E infection and pregnancy is a deadly and fatal combination. Specifically, in 3rd trimester of pregnancy, acute hepatitis E has a grave prognosis with high maternal morbidity and mortality. Prevention is the mainstay of controlling HEV especially in developing countries.

Keywords: Hepatitis E, Hepatic failure, DIC, Pregnancy

INTRODUCTION

Hepatitis E is an inflammation of liver caused by infection with the hepatitis E virus (HEV).[1]

Each year, estimated 20 million hepatitis E infections are diagnosed worldwide; from whom, over 3.3 million are symptomatic cases and these cases accounting for approximately 44,000 deaths in 2015 (3.3% of mortality due to viral hepatitis).[1]

Viral hepatitis is considered as the most common cause of Jaundice in pregnant women and this pregnancy is considered as a high-risk pregnancy.

Hepatitis E is a single stranded RNA virus (HEV). It is of 4 different type: genotype 1, 2, 3 and 4.[1]

Genotype 1 and 2 has been found in humans. Genotypes 3 and 4 viruses circulate in animals, without causing any disease and occasionally infect humans (as humans can get infected by eating infected animal meat).[1]

Hepatitis E virus is spread by feco-oral route. The virus is

shed in the stools of the infected persons. It is mainly transmitted through contaminated drinking water.[1,2]

The disease has low case fatality rate (<0.1%) in non-pregnant women as compared to its infection in pregnancy, where it is responsible for high maternal mortality rate (15-30%) and higher perinatal mortality rate (40-50%) particularly in third trimester.[3] Mother to child transmission may occur either due to vertical transmission in-utero or during delivery.

Management of HEV infection during pregnancy is usually similar to managing jaundice due to other causes of viral hepatitis. Immuno-prophylaxis is under trial.

Studies carried out in India, Iran, Africa and middle east have found to have higher incidence of fulminant hepatitis in pregnancy especially in third trimester.[4]

This study was carried out to evaluate the adverse effect of HEV infection during pregnancy, it's effect over maternal outcome and fetal outcome.

METHODS

This is a retrospective observational study that was carried out in L.G. hospital from 1st May 2020 to 30th April 2021 in which the course of the disease and socio-demographic patterns and feto-maternal outcome were studied in the pregnant patients having HEV infection during third trimester of pregnancy.

Inclusion criteria

All the patients included in this study were ≥18 years of age. The patients having HEV infection only during their third (3rd) trimester of pregnancy were included. All these patients were having singleton pregnancy.

Exclusion criteria

Patients having age of more than 35 years were excluded. All the patients with multi-fetus pregnancies were excluded. Patients having any other medical disorders were excluded from our study. Any pregnancy with mal-presentation was not included. Patients with parity>3 were excluded.

Analysis of 50 patients regarding age, parity, socio-economic class, residential status, pregnancy outcome, obstetric outcome, maternal and perinatal morbidity and mortality etc. was done. All data were collected from case collection.

All the pregnant patients with the HEV infection were admitted as well as thorough the investigations were carried out.

These investigations included complete blood count, liver function test, renal function test, coagulation profile, serum viral markers, serum electrolytes, maternal USG abdomen and pelvis, fetal ultra-sonography. Investigations were repeated whenever required.

Conservative management or "wait and watch" policy was followed when patient showed sign of clinical and laboratory indices improvement. Majority of the patients were in labour when admitted and delivered spontaneously. Induction of labour was done in selected cases to prevent maternal and perinatal morbidity and mortality.

Decisions for operative deliveries were taken for obstetrical indications like obstructed labour and history of previous operative deliveries. Help of neonatologist was also taken whenever needed.

Ethical approval not required and statistical analysis done by Microsoft excel.

RESULTS

In this study, total 50 patients infected with HEV during their 3rd trimester of pregnancy were included.

All the patients included in this study were between18 years to 35 years of age.

Table 1: Month of admission during HEV infection, (n=50).

Months	No. of patients	Percentage (%)
January	2	4
February	2	4
March	2	4
April	1	2
May	0	0
June	3	6
July	2	4
August	9	18
September	9	18
October	8	16
November	8	16
December	4	8

In this study, maximum numbers of HEV infected patients were seen during the month of August (18%) and November (18%) followed by September (16%) and October (16%). This shows that in monsoon season, there is higher chance of fecal contamination of drinking water when there is leakage of sewage pipes and mixing with drinking water. Saeedi et al observed HEV outbreaks were more common during monsoon and summer months.[5]

In this study, numbers of emergency admission were 35 out of 50 (70%) and numbers of registered patients were 15 out of 50 (30%).

Table 2: Emergency or registered patients, (n=50).

Patient status	No. of patients	Percentage (%)
Emergency patients	35	70
Registered patients	15	30

All emergency patients were referred from either private hospitals or PHCs, CHCs and other referral hospitals in the later stages of the diseases, as our institute is a tertiary care centre.

Table 3: Socio-economic status of the patients, (n=100).

Socioeconomic-status	Present study percentage (%)	Rachana percentage (%)[6]
Low	82	80
Middle	18	20

In patients belonging to lower socio-economic class, lack of awareness about mode of transmission of infection, poor quality of life, poor hygienic habits and poor sanitation practices were the contributing factors for HEV infection. This finding is co-relatable to the Kumar et al study.[10]

Table 4: Residential status of the patients, (n=50).

Residential status	No. of patients	Percentage (%)
Urban	38	76
Rural	12	24

In this study, patients from urban areas were 38 (76%) and from rural areas were 12 (24%). Our institute is located in urban region, more than half of the patients were belonging to urban regions. So, most of these patients were from urban areas. As our institute is tertiary care centre, patients were referred from nearby rural areas as well.

In this study, 15 (30%) patients had S. bilirubin level <5 mg/dl, 11 (22%) patients had S. bilirubin level between 5.1-10 mg/dl, 16 (32%) patients had S. Bilirubin between 10.1-15 mg/dl and 8 (16%) patients had S. bilirubin >15 mg/dl. ALT or SGPT was raised in 32 (64%) and serum alkaline phosphatase was raised in 32 (64%) patients of 50 HEV pregnant females.

As HEV infection mainly affects the liver and get abnormal leads to acute fulminant hepatitis, coagulative function may get abnormal. In this study, PT and APTT were raised in 56% of patients. FDP was raised in 70% of patients.

Out of 50 HEV positive patients, 1 (2%) had HAV infection along with HEV infection and 2 (4%) had HBV infection along with HEV infection.

Table 5: Results of the various investigations, (n=50).

Investigation	Values	No. of patient	Percentage (%)
Hemoglobin (gm/dl)	<7	2	4
	7.1-9	10	20
	9.1-11	28	56
	>11	10	20
Total WBC count (cumm)	<11000	28	56
	>11000	22	44
Platelets (cumm)	<1,00,000	10	20
	>1,00,000	40	80
S. bilirubin (mg/dl)	<5	15	30
	5.1-10l	11	22
	10.1-15l	16	36
	>15	8	16
SGPT (ALT) (Normal 0-55 U/L)	<100	18	36
	100-1000	26	52
	>1000	6	12
ALP (Normal 50-150 U/L)	<150	18	36
	≥150	32	64
Prothrombin time (PT)	Normal	22	44
	Raised	28	56
Activated partial thrombo-plastin time (APTT)	Normal	22	44
	Raised	28	56
Fibrin degradation product (FDP)	Normal	15	30
	Raised	35	70

Table 6: Co-infection with other hepatitis virus, (n=50).

Investigation (Viral markers)	No. of patients	Percentage (%)
HAV infection	1	2
HBV infection	2	4
HCV infection	-	0
HEV infection	50	100

Table 7: Mode of delivery, (n=50).

Mode of delivery	No. of patients	Percentage (%)
Vaginal delivery	38	76
LSCS	11	22

In present study, out of 50 HEV infected pregnant females, 1 patient died antenatally, patients delivered vaginally were 38 (76%). From that, pre-term vaginal delivery (<37 weeks) was 24(48%) and full-term vaginal delivery (>37 weeks) in 14 (28%) of cases.

Table 8: Maternal complications in pregnant female with HEV infection.

Complications	Present study		Shinde et al study[7]	
	N	%	N	%
DIC	13	26	22	42
Low platelet count	10	20	-	-
PPH (Atonic + traumatic)	9	18	9	17.30
Hepatic encephalopathy	8	16	24	46
Fever	6	12	12	23.07
Septicemia	4	8	-	-
Acute renal failure (ARF)	2	4	11	21
Wound complications	4	8	-	-

In this study, most common complication in HEV infected pregnant female was DIC in 13 (26%), low platelet count in 10 (20%), PPH in 9 (18%) patients including both atonic and traumatic PPH, hepatic encephalopathy in 8 (16%) patients out of 50 HEV infected pregnant females.

As per WHO, pregnant women with hepatitis E, particularly those in 2nd and 3rd trimester, are at increased risk of acute liver failure, fetal loss and mortality.[1]

Shinde et al study had DIC in 42%, PPH in 72%, ARF in 21%, hepatic encephalopathy in 26% and fever in 23.07% of patients.[7]

Table 9: Perinatal outcome, (n=50).

Outcome of baby	No. of patients	Percentage (%)
Live birth	42	84
IUFD (intra-uterine fetal death)	8	16
Meconium-stained liquor at birth	6	12
Pre-term birth	24	48
RDS (respiratory distress syndrome)	10	20
NICU admission	36	72
Early neonatal death	6	12
Late neonatal death	4	8

In this study, out of 50 patients, babies born alive were 42 (88%), IUFD were 8 (16%), pre-term births were 24 (48%), and NICU admissions were needed for 36 (72%) babies. Early neonatal death was in 6 (12%) and late neonatal death was in 4 (8%) of cases. Perinatal mortality is as high as 14 (28%) in this study.

As per Shreshta et al, preterm delivery was as high as 67%, still birth in 11% and perinatal mortality was 20.2%.[8]

Table 10: Comparison of maternal mortality due to HEV infection with other studies.

Study	Years	Percentage (%)
Prasad et al[9]	2015	20.8
Kumar et al[10]	2016	21.88
Javed et al[11]	2017	14
WHO[1]	2021	20-25
Present study	2020-21	14

In this study, maternal mortality in HEV infected pregnant females is 14%. As per WHO, pregnant women with HEV are at greater risk of severe complications and mortality in 3rd trimester of pregnancy.[1]

DISCUSSION

In present study, 50 cases with HEV infection in 3rd trimester of pregnancy were included from 1st May 2020 to 30th April 2021. Max numbers of HEV infected patients seen during later half of year, i.e., from July-December. This data is comparable with Saeedi et al study.[5]

Patients from urban areas were 38 (76%) and from rural areas were 12 (24%). Our institute is located in a metropolitan city, so more patients were from urban areas. But patients were referred from peripheral areas and nearby PHCs also.

Majority of patients belong to lower socio-economic class (82%), which is comparable to findings of Rachana et al study (80%).[6] This suggests HEV is more commonly seen in lower socio-economic class, as their lack of awareness about transmission of disease, poor sanitation and hygiene, poor quality of life contributing factors for HEV infection.

Emergency patients were 35 (70%) and registered patients were 15 (30%). Because our institute is a tertiary care centre, patients were referred from PHCs, CHCs and other private hospitals.

In this study, 15 (30%) patients had S. bilirubin level <5 mg/dl, 27 (54%) patients had S. bilirubin level between 5.1-15 mg/dl and 8 (16%) patients had S. bilirubin >15 mg/dl. ALT or SGPT was raised in 32 (64%) and serum alkaline phosphatase was raised in 32 (64%) patients of 64 HEV pregnant females. PT, APTT, FDP were altered in 22 (44%), 22 (44%) and 15 (30%) patients respectively.

In this study, out of 64 HEV infected pregnant females, patients delivered vaginally were 38 (76%), delivered by LSCS were 11 (22%).

In this study, most common complication observed in HEV infected pregnant female was DIC in 13 (26%), other common complications encountered in HEV infected pregnant female were low platelet count in 10 (20%), PPH in 9 (18%), hepatic encephalopathy in 8 (16%), septicemia in 4 (8%), Acute renal failure in 2 (4%) patients. Ventilator support was needed in patients with hepatic

encephalopathy. Shinde et al study had DIC in 42%, PPH in 72%, ARF in 21%, hepatic encephalopathy in 26% and fever in 23.07% of patients.[7]

Maternal mortality rate in our study is 14% (7 patients out of 50). Out of 7 mortalities, 6 occurred in emergency patients. 1 patient died antenatally.

In present study, out of 50 patients, babies born live were 42 (84%), IUFD were 8 (16%), MSL were 6 (12%), and preterm babies were 24 (48%). NICU admission was needed in 36 (72%) babies. Perinatal mortality rate was as high as 28%.

Limitations

In this study, only patients with 3rd trimester of pregnancy with HEV infection have been monitored. Also, co-infection with other hepatitis infection were included, which further adverse the disease.

CONCLUSION

Hepatitis E infection and pregnancy is deadly and fetal combination specifically 3rd trimester of pregnancy, acute hepatitis E has a grave prognosis with very high maternal morbidity like DIC, fulminant hepatic failure, hepatic encephalopathy, PPH etc. There is high risk of IUFD and stillborn, fetal distress, meconium aspiration syndrome, higher perinatal morbidity and mortality.

Prevention is mainstay of controlling HEV infection especially in developing countries. As HEV infection is highly prevalent in lower socioeconomic class people and these people have lower education level, all the antenatal women and their family members should be educated and made aware about different modes of transmission of HEV, symptom and signs and importance of good hygiene and sanitation habits through various government programmes and skit/pictures education. Routine antenatal care and early recognition and detection of HEV Infection among pregnant female is must to reduce maternal morbidity and mortality. Aggressive management is must and it should be done at tertiary care center with multi-disciplinary approach, these can reduce maternal morbidity and mortality along with perinatal mortality.

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