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Original Research Paper

Gynaecology

STUDY OF FETO-MATERNAL OUTCOME IN MATERNAL HEPATITIS E INFECTION DURING PREGNANCY

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ABSTRACT The present study was conducted to study the incidence, etiology & Feto-Maternal outcome in pregnant female with HEV infection. It was a retrospective observational study at atertiary care institute from 1st february2019 to 31st july2019. Total of 15 cases of HEV infection in pregnancy were found during this period.

Result:- 80% patients belong to lower socioeconomic class. Most common complications seen were generalized weakness and yellowish discoloration of sclera seen in 100% & 93.33% respectively. DIC was seen in 66.66%. 2 patients died & case fatality ratio was 13.33%.

KEYWORDS :

INTRODUCTION

- Hepatitis E is a liver disease caused by a virus known as Hepatitis E Virus (HEV).1
- Each year, estimated 20 million hepatitis E infections are diagnosed worldwide; over 3.3 million symptomatic cases, 44000 Deaths in 2015, accounting for 3.3% of mortality due to viral hepatitis & 3000 Still Births annually are related to HEV infections.1
- Viral hepatitis is the most common cause of Jaundice in pregnant women and is considered as a High Risk Pregnancy.
- Hepatitis E is the Single Stranded RNA virus (HEV), with at least 4 different type: - Genotype 1, 2, 3, 4 & is spread by FECO-ORAL Route like hepatitis A Virus. The virus is shed in the stools of the infected persons. It is mainly transmitted through contaminated drinking water.1,2,3,4,5
- Its specific diagnosis depends on the detection of specific serological markers which are HEV IgM & IgG for Acute & Chronic hepatitis status respectively.1,2,3,4,5
- The disease has low case fatality rate (<0.1%) in Non-Pregnant women & in pregnancy the maternal mortality rate is (15-30%) perinatal mortality rate (40-50%) particularly in third trimester.6 Mother to child transmission may occur either due to vertical transmission in-utero or during delivery.
- Overall management of HEV during pregnancy is similar as managing jaundice due to other causes of viral hepatitis.

INCLUSION CRITERIA:-

All the pregnant HEV positive female.

CLINICAL PRESENTATION

The incubation period ranges from 2-10 Weeks.1
The course of HEV infection has 2 phases,

1. The prodromal phase
2. The icteric phase.

Prodromal phase symptoms lasts 1-4 days & include the following2:

- Nausea & vomiting (30-100%)
- Anorexia (66-100%)
- Fever with mild temperature elevations (25-97%)
- Weight loss (typically 2-4kg)
- Right upper quadrant pain that increases with physical activity (abdominal pain is reported in 35-80% of patients)
- Myalgia
- Arthralgia
- Dehydration
- Most prodromal symptoms tend to diminish with the onset of jaundice (icteric phase), but dark urine, light stool colour and itching persist for a varying amount of time.

Icteric phase symptoms may last days to several weeks and include the following2:

- Jaundice - May be difficult to see with some patient's natural skin color; serum billirubin level is usually higher than 3mg/dl; scleral icterus is present; usually occurs between the 5th-8th week after infection
- Dark urine
- Pruritus (50%)
- Light-colored stools (20-40%)

Other features include the following7,8:

- Malaise (most common)
- Thrombocytopenia
- Aplastic anemia

COMPLICATIONS

- **In Mother:-**
- Fulminant hepatic failure occurs in 75% of the pregnant patients infected with HEV in 3rd trimester9.
- Metabolic Alterations: impaired hepatic glycogenolysis and or gluconeogenesis, hypokalemia and hypophosphatemia10.
- Disseminated intravascular coagulation because of impaired production of clotting factors and vitamin k leading to multiple organ failure.
- Thrombocytopenia due to platelet consumption.
- Hepatic encephalopathy occurs due to transfer of ammonia from intestine to brain bypassing the liver because of hepatic failure.
- Ascites
- Increased risk of preterm labour.
- Antepartum haemorrhage (APH), Postpartum haemorrhage (PPH) Wound gap hematoma may follow impaired coagulation.

- **In Fetus and Neonate**
- Hepatitis E during pregnancy is also associated with higher rates of IUD, prematurity and its complications like respiratory distress syndrome (RDS), asphyxia neonatorum (ANN) and jaundice, low birth weight and an increased risk of perinatal mortalitY1.

DIAGNOSIS

1. HISTORY1,2:-

- As HEV infection is food borne disease, a detailed history regarding drinking water & its source, food taken (undercooked meat etc.), contact with jaundiced persons should be included in history.

2. PHYSICAL EXAMINATION1,2:-

- Per abdominal examination reveals gravid uterus.

- Due to liver involvement, there may be presence of enlarged liver, which may be soft & slightly tender. Some may have splenomegaly and Ascites.

3. ULTRASONOGRAPHY1,2:-
- Abdominal ultrasonography is recommended. It may also demonstrate the presence of an enlarged liver and the presence of advanced liver disease, such as Ascites, hepatomegaly, splenomegaly, or hepatofugal flow of the portal venous system.
- It indicates fetal growth and well being.

4. LABORATORY TEST ABNORMALITIES1,2:-
- Elevation of AST, ALT, ALP and other liver enzymes. Serum bilirubin level usually ranges from 5-20 mg/dl, depending on the extent of hepatocyte damage. It returns to normal level by 6 weeks.
- Prolonged prothrombin time, decreased serum albumin, and very high bilirubin are signs of impending hepatic failure requiring referral to a liver transplantation centre.

5.SEROLOGICAL STUDY1,2:-
- -ELISA is used for the detection of Anti-HEV IgM Ab, and Anti-HEV IgG Ab. IgM Ab usually start rising 4 weeks after infection and remains detectable for 2 months after the onset of infection.3
- Two specialized test require specialized laboratory facilities & are used only in research studies1,2. These tests are:
- RT-PCR (reverse transcriptase polymerase chain reaction) to detect the hepatitis E virus RNA.
- Electron microscopy used to detect HEV virus.

MANAGEMENT

1. PREVENTION:-
- Management is mainly focused on prevention, because prevention is the best treatment for the diseases like HEV infection.1,2,3
- The risk of HEV infection and its transmission can be reduced By1,2,3.
- Maintaining quality standards for public water supplies.
- Establishing proper disposal systems to eliminate sanitary waste.
- Maintaining proper hygienic practices such as hand washing with safe water, particularly before handling the food.
- Avoiding uncooked shellfish & avoid eating animal meat that could possibly transmit HEV.
- Inactivation HEV virus can be achieved by boiling and chlorination of water.

2. TREATMENT11:-
- Hepatitis E usually resolves on its own without treatment.
- There is no specific antiviral therapy for Hepatitis E. Hence supportive therapy is advocated.
- Patients are advised to get adequate rest, nutrition and fluids.
- Hospitalization should be considered for pregnant women for thorough investigation and better management to prevent morbidity and mortality. Isolation of infected pregnant patients is not indicated, because person-to-person transmission is uncommon.

3. SUPPORTIVE TREATMENT11:-
- Higher antibiotics if patient is having high WBC count.
- Syrup Lactulose (15-30ml) should be given three times daily as an osmotic laxative and reduces colonic ammonia absorption which is harmful to the brain as ammonia can lead to hepatic encephalopathy.
- Ursodeoxycholic acid in oral form for conjugation of toxic products of metabolism of billirubin.

4. MANAGEMENT IN PREGNANCY:-
- Therapeutic termination of pregnancy and its beneficial effects have not been fully explored in HEV infection12.
- Hence conservative management or "WAIT & WATCH" policy should only be chosen if the patients show signs of clinical and laboratory indices improvement13.

5. MANAGEMENT DURING LABOUR11:-
- Vaginal delivery is preferred mode of delivery. Caesarean section should be done only for obstetric indication.
- In the patients with altered coagulation profile & hemorrhage, blood and blood components like FFP, cryoprecipitate and platelets are given. Vitamin K 5mg must be administered I/M to raise prothrombin level.

RESULTS AND OBSERVATION

TABLE 1:- SOCIO-ECONOMIC STATUS OF THE PATIENTS

Socio-economic status	Present Study	Rachna Et Al14 Study
	Percentage (%)	Percentage (%)
Low	80%	80%
Middle	20%	20%

Patients belonging to lower socio-economic class were 12 (80%) & from middle socio-economic class were 3 (20%) which is comparable to the study of Rachana M Kumar Et al14 who had also reported above 80% pregnant patients infected with HEV were from lower socio-economic class.

TABLE 2:- SYMPTOMS AND SIGNS OF THE PATIENTS

Signs & Symptoms	Present Study		NR Shinde et al Study 15	
	No. of patients/15	Percentage (%)	No. of patients/52	Percentage (%)
Generalized weakness	15	100%	52	100%
Yellow discoloration of urine and sclera	14	93.33%	35	67.3%
Abdominal Pain	9	60%	-	-
Nausea & vomiting	12	80%	52	100%
Loss of appetite	15	100%	-	-
Swelling over feet or body	6	40%	-	-
Altered sensorium	3	20%	11	21.1%
Pruritus	4	26.66%	6	11.5%
Hepato-Splenomegaly	4	26.66%	-	-

Most common symptom was generalized weakness in 15 (100%), yellowish discolouration of sclera & urine in 14 (93.33%), abdominal pain in 9 (60%), nausea & vomiting in 12 (80%), loss of appetite in 15 (100%), swelling of feet and body (oedema) in 6 (40%), altered sensorium in 3 (20%), pruritus in 4 (26.66%) hepato-splenomegaly in 14 (26.66%) patients out of 15 patients.

In study by NR Shinde Et al15, most common presenting symptom was nausea & vomiting in 100%, yellowish discoloration of sclera & urine in 86.5%, DIC in 42%, altered sensorium in 21.1% & pruritus in 11.5% patients of 52 HEV pregnant females.

Data from my study is comparable with the data of study by NR Shinde et al15.

TABLE 3:- RESULTS OF VARIOUS INVESTIGATIONS

Investigation	Values	Present Study		Bina R Et Al Study16	
		No. of patients / 15	Percentage (%)	No. of patients/15	Percentage (%)
S. Billirubin (Normal 0.2-1.2 mg/dl)	<5 mg/dl	6	40%	16	30.77%
	5.1-10 mg/dl	4	26.66%	8	15.38%
	10.1-15 mg/dl	3	20%	18	34.61%
	>15 mg/dl	2	13.33%	10	19.23%
SGPT (ALT) (Normal 0-55 U/Litre)	<100 U/L	2	13.33%	18	34.61%
	100- 1000 U/L	10	66.66%	28	53.85%
	>1000 U/L	3	20%	6	11.54%

ALP (Normal 50-150 U/ Litre)	<150 U/L	6	40%	16	30.77%
	>150 U/L	9	60%	36	69.23%
Prothrombin Time (PT)	Normal	6	40%	36	69.23%
	Raised	9	60%	16	30.77%
Activated Partial Thromboplastin Time (APTT)	Normal	6	40%	36	69.23%
	Raised	9	60%	16	30.77%
Fibrin Degredation Product (FDP)	Normal	5	33.33%	37	71.15%
	Raised	10	66.66%	15	28.85%
D-Dimer	Normal	3	20%	37	71.15%
	Raised	12	80%	15	28.85%

In my study, 6 (40%) patients had S.Billirubin level <5 mg/dl, 7 patients had S.Billirubin level between 5.1-15 mg/dl & 2 (13.33%) patients had S.Billirubin >15 mg/dl. ALT or SGPT was raised in 86.66% & Serum alkaline phosphatase was raised in 60%, PT & APTT were raised in 9 (60%) of patients. FDP was raised in 10 (66.66%). D-dimer was raised in 12 (80%) & HEV was positive in 15 (100%) patients of my study.

In study by Bina R Et al16, 16 (30.77%) patients had S.Billirubin level <5 mg/dl, 26 (50%) patients had S.Billirubin level between 5.1-15mg/dl & 10 (19.23%) patients had S.Billirubin >15 mg/dl. ALT was raised in 34 (65.39%) and Serum alkaline phosphatase was raised in 36 (69.23%). PT & APTT were raised in 30.77% of patients, d-dimer was positive in 71.15% of patients. This study consists of 52 HEV positive pregnant females. Data from my study is nearly comparable with the data of study by Bina R et al16.

TABLE 4:- MODES OF DELIVERY

MODE OF DELIVERY	Present Study		GS Prasad Et Al Study17	
	No. of patients/15	Percentage (%)	No. of patients/15	Percentage (%)
Vaginal Delivery	12	80%	46	85.18%
LSCS	3	20%	8	14.81%

In my study, out of 15 HEV infected pregnant females, number of patients delivered vaginally were 12 (80%), delivered by LSCS were 3 (20%) out of 15. Study by GS Prasad et al17 had vaginal delivery rate of 85.18% (46 out of 54 patients) and LSCS rate of 14.81% (8 out of 54 patients). Abortion rate was of 1.81% (1 out of 55 patients).

TABLE 5:- MATERNAL COMPLICATIONS IN PREGNANT FEMALE WITH HEV INFECTION

Complications	Present Study		N R Shinde15 et al Study	
	No. of patients/15	Percentage (%)	No. of patients/52	Percentage (%)
DIC (Disseminated Intravascular Coagulation)	10	66.66%	22	42%
PPH (Atonic + Traumatic)	3	20%	9	17.30%
Hepatic Encephalopathy	2	13.33%	24	46%
Septicaemia	2	13.33%	-	-
Acute Renal Failure (ARF)	1	6.66%	11	21%
Wound Complications	1	6.66%	-	-

In my study, most common complication in HEV infected pregnant female was DIC (Disseminated Intravascular Coagulation) 10 (66.66%), PPH in 3 (20%) patients including both atonic & traumatic PPH, hepatic encephalopathy in 2 (13.33%) patients out of 15 HEV infected pregnant females. Ventilator support was needed in patients with hepatic encephalopathy. Septicaemia was seen in 2 (13.33%), acute renal failure in 1 (6.66%) patients. Multiple complications were seen together in some patients. Blood components were given to 12 (80%) of patients. 2 patients died.case fatality rate was 13.33%.

Study by NR Shinde et al15 had DIC in 42%, Ascites in 26%, ARF in 21%, hepatic encephalopathy in 46%, fever in 23.07% patients. Data from my study is also comparable with the data of study by NR Shinde et al15.

TABLE 6:- PERINATAL OUTCOME

Outcome Of Baby	No. of patients/15	Percentage (%)
Live Birth	12	79.68%
IUFD (Intrauterine Fetal Death)	3	18.75%
Meconium Stained Liquor At Birth	4	15. 63%
Preterm	11	56.25%
RDS (Respiratory Distress Syndrome)	3	20. 31%
NICU admission	7	34. 38%
Early Neonatal Death	2	12.5%
Late Neonatal Death	1	9.38%

In my study, out of 15 patients, babies born live were 12 (60%), IUFD were 3 (20%), MSL were 4 (26.66%), and preterm babies were 11 (73.33%). NICU admission was needed in 7 (46.66%) babies. Perinatal mortality rate was as high as 20%. In study by GS Prasad Et al17, live born babies were 95.91%, still birth were 4.08%, MSL were 8.51%, preterm babies were 80.85%, NICU admission needed in 40.42% and perinatal mortality rate was 4.25%. Studies by NR Shinde Et al15 reported perinatal mortality rate of 23.1%.

CONCLUSION

Hepatitis E infection and pregnancy is a deadly & fatal combination. Specifically in 3rd trimester of pregnancy, acute hepatitis E has a grave prognosis with very high maternal morbidities like DIC, Fulminant Hepatic Failure, Hepatic Encephalopathy, PPH etc. It accounts for a significant number of deaths and increases the maternal mortality rate of the country.

There is higher risk of preterm delivery, IUFD & still born, fetal distress, Meconium aspiration syndrome, higher perinatal morbidity and mortality.

Unlike other diseases such as HIV which has multiple routes of transmission, HEV has a feco-oral route of transmission and hence the disease burden can be lessened by ensuring better sanitation and provision of clean drinking water for pregnant women.

Prevention is the mainstay of controlling HEV infection especially in developing countries. As HEV infection is highly prevalent in lower socio-economic class people & these people have lower educational level, all the antenatal women and their family members should be educated and made aware about different modes of transmission of HEV, symptom & signs and importance of good hygiene & sanitation habits through various government programmes and skit or picture education. Routine antenatal care and early recognition & detection of HEV infection among pregnant females and its aggressive management is must to reduce maternal morbidity & mortality.

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