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Original Research Article

Pregnancy outcome with hepatitis E infection

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ABSTRACT

Background: Hepatitis E is usually a self-limited viral infection in men and non-pregnant women, but during pregnancy it is associated with high maternal and perinatal mortality. This needs to be studied for early diagnosis and better management.

Methods: The study commenced after the approval of Institutional Ethics Committee. This was a retrospective cum prospective observational study conducted in the Department of Obstetrics and Gynaecology and Department of Medical Intensive Care Unit in present tertiary care hospital between February 2012 and July 2017. An analysis of 120 cases was made over a period of five years.

Results: In this study the incidence of pregnant patients with hepatitis E was 3.09 per 1000 deliveries. It was found that majority of the patients which were diagnosed with hepatitis E were young and belonged to the age group of 21-25 years. Most of the affected patients were primigravida with increasing severity of the disease in their third trimester. The maternal morbidity was 51% with a mortality rate of 20%. The percentage of still birth was 25.64% with increased incidence of preterm deliveries and poor perinatal outcome.

Conclusions: Early diagnosis and rapid management of the complications such as correction of abnormal coagulation and supportive management is the best treatment available at present. ICU admission and with strict maternal and foetal monitoring can help improve the outcome and thereby reducing the maternal and perinatal mortality.

Keywords: Hepatitis E, Maternal mortality, Perinatal mortality, Severe acute maternal morbidity, Viral hepatitis

INTRODUCTION

Acute viral hepatitis is an infection which predominantly affects the liver but can also lead to multiorgan failure. It is usually self-limited liver disease with a serum aspartate aminotransferase elevation of at least five-fold or clinical jaundice or both.¹ Most of the cases of acute viral hepatitis are caused by one of five viral agents: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV).

Hepatitis E infection is found to be a major cause of viral hepatitis all over the world. According the WHO review

in the year 2017, there are approximately 20 million hepatitis E infections yearly, and 3.3 million symptomatic cases. Approximately 70,000 deaths per year have been attributed to HEV genotypes 1 and 2 and the estimated mortality is about 3.3%. Case-fatality rates in highly endemic areas have ranged from 0.5% to 4% in hospital-based data and 0.07% to 0.6% in population surveys during outbreaks.² Hepatitis E is usually self-limited in men and non-pregnant women, but during pregnancy it is associated with high maternal mortality.³ Malnutrition superimposed on the normal demands of pregnancy and inversion of T and B lymphocytes in early pregnancy have been postulated to be the contributing factors for high level of incidence and complications.

In pregnancy because of lower immune status, there is increased risk for viral replication which leads to higher case fatality rate among the pregnant women as compared to the general population.

Studies show that during outbreaks of waterborne hepatitis E in India and Asia the case-fatality rate was 1-2% in general population and up to 10-20% in pregnant women. Mortality rates among pregnant women, especially those infected in the third trimester, have ranged between 15% and 25%, much higher than men and non-pregnant women.⁴

It has been reported that a significant proportion of pregnant women with acute hepatitis E progress to acute liver failure with a short pre-encephalopathy period, rapid development of cerebral oedema and high occurrence of disseminated intravascular coagulation.⁵ Hepatitis E in pregnancy is also associated with high rates of spontaneous abortion, intrauterine death, and preterm labour.

Prematurity in newborns and fulminant hepatic failure in mothers are major cause of poor fetomaternal outcome in acute hepatitis E with pregnancy.⁶ Hence authors have taken up this study for finding out ways for a better maternal and foetal outcome.

METHODS

The study commenced after the approval of Institutional Ethics Committee. This was a single centre observational study. A retro prospective analysis of hospital record of all obstetric cases with hepatitis E admitted in department of obstetrics and gynecology and medical intensive care unit at a tertiary care hospital was done over a period of five years.

Inclusion criteria

- All pregnant women admitted in present tertiary care centre with blood laboratory test showing positive titres only for active hepatitis E (IgM Hep-E) in the current pregnancy in their antenatal period or up to 42 days post-delivery were included in the study.

Exclusion criteria

- Pregnant women with laboratory tests showing positive titre for other viral type of Hepatitis or with any other cause of jaundice were excluded.

The retrospective analysis of hospital record of all cases with hepatitis E admitted in Department of Obstetrics and Gynecology and medical intensive care unit at a Tertiary care hospital was done and details were noted down in data record form. There was no patient interaction involved. Cases were seen from hospital records and wavier of consent was taken.

Data was collected from history and case records for these cases. In the prospective part of the study data of the patients who were newly diagnosed with Hepatitis E, their informed consent was taken and case history, investigations and maternal and fetal outcome were recorded. Since it was an observational study, findings were noted in the case record form. A comparison was done considering various demographic and medical parameters such as age of the patient, parity, gestational age, delivery mode, admission in critical care unit, presenting symptoms, complications and the perinatal outcome. Results were compared with percentage calculations.

RESULTS

Incidence

In this study total 120 cases of hepatitis E were observed. During the study period there were total 38817 deliveries in the tertiary care centre, and the incidence calculated was 3.09 per 1000 deliveries.

Maternal parameters

Age

According to Table 1 the maximum percentage of patients affected belonged to the age group of 21 to 25 years which was 47.52% of the total number of patients, followed by the age group between 26 to 30 years which contributed 41.66%.

Table 1: Age groups of patients diagnosed as hepatitis E positive.

Age	No. of cases	Percentage
<20	2	1.66
20-25	57	47.52
26-30	50	41.66
>30	11	9.16
Total	120	100

Out of total 120 cases found majority were diagnosed to be hepatitis E positive in their third trimester, while very few were infected in the first and the second trimester. Analyzing this it shows that patients are more affected in their third trimester.

Table 2: Distribution according to the trimester of pregnancy.

Duration of pregnancy (gestational age in weeks)	No. of cases	Percentage
1 st trimester (up to 12weeks)	2	1.67
2 nd trimester (13-27weeks)	15	12.50
3 rd trimester (28 and above)	103	85.83
Total	120	100

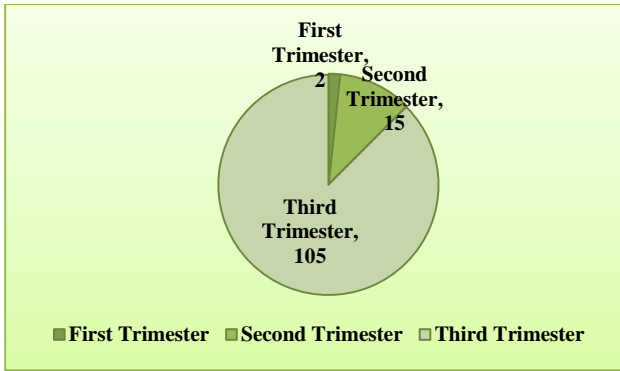


Figure 1: Distribution according to the gestational age.

Clinical presentation

The most common presenting symptom was jaundice i.e. either yellowish discoloration of skin or sclera or dark urine. Almost 92.5% of the affected individuals had jaundice.

Table 3: Clinical presentation on admission.

Clinical presentation at time of admission	No. of cases
Fever	50
Loss of appetite	10
Nausea/ vomiting	25
Myalgia/ arthralgia	3
Jaundice	111
Pruritis	5
Diarrhoea	7
Altered sensorium	15
Others	4

The second most common complaint was fever seen in about 41.6% of the patients, followed by nausea and vomiting. Pictorial description of the presenting symptoms is given in Figure 2.

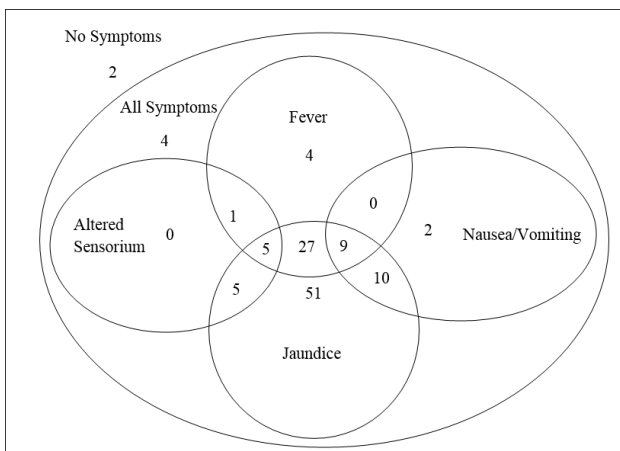


Figure 2: Presenting symptoms.

Onset of labour

According to available data 77.5% of the patients went into spontaneous labour, while 16.67% had to be induced. Among the remaining patients two had spontaneous abortion in their first trimester, one patient underwent an elective lower segment caesarean section in view of previous two lower segment caesarean sections, three patients died undelivered, while one patient was postnatal whose details regarding labour were not available.

Table 5: Onset of labour.

Labour	No of cases
Spontaneous	93
Induced	20

There were total 120 cases out of which 115 delivered, 3 patients died undelivered and 2 patients had spontaneous abortion. Out of total 115 patients delivered 100 patients delivered vaginally and 15 underwent lower segment caesarean section. Vaginal delivery is preferred over operative interventions in these patients because of increased risk of bleeding and morbidity due to abnormal coagulation.

Table 6: Mode of delivery.

Mode of delivery	No. of cases
Vaginal delivery	100
Caesarean section	15
Spontaneous Abortion	2
Undelivered	3

Maternal outcome

Maternal outcome has been analyzed as number of morbid cases, total number of patients requiring admission into intensive care setups and number of mortalities.

Maternal morbidity

Table 7: Morbid conditions.

Maternal morbidity	Frequency
Hepatic encephalopathy	34
Deranged coagulation profile	61
Post-partum haemorrhage	6
Renal failure	3

There were total 62 cases with morbid condition. Out of these 62 patients, 38 survived and 24 patients died. Out of total 62 patients, 61 patients had abnormal coagulation profile, 34 patients had hepatic encephalopathy, 6 patients post-partum haemorrhage and 3 patients had hepatorenal involvement. Pictorial representation of the same is given in Figure 3.

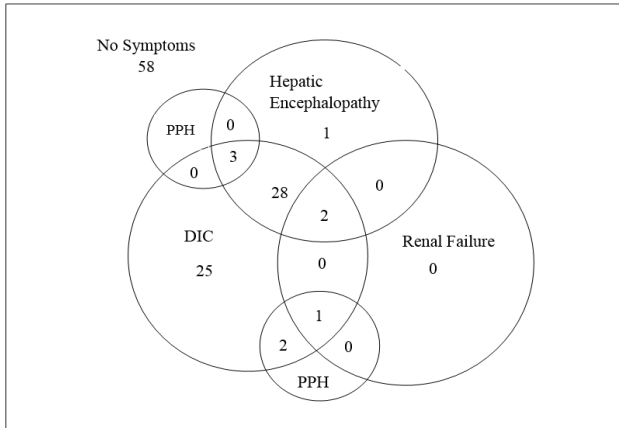


Figure 3: Complications.

Need for intensive care unit admission

A total of 79 patients out of 120 required admission in medical intensive care unit which is 66% of the total number of patients with hepatitis E.

Maternal mortality

Out of total 120 patients there were total 24 maternal mortalities. The percentage of mortality was approximately 20%.

Comparative analysis of the investigative parameters between the survivors and the non-survivors

Table 8: Maternal survival.

Investigation	Survivor	Non-survivor
Total number of patients	96	24
Median haemoglobin (mg%)	11	8.5
Median TLC (mm ³)	13000	18350
Median platelet (lacs)	2.15	1.8
Median of SGOT (IU)	358.26	1520.50
Median of SGPT (IU)	268	1115
Median total bilirubin (mg/dl)	7.60	13.1
Median INR	1.26	4.1

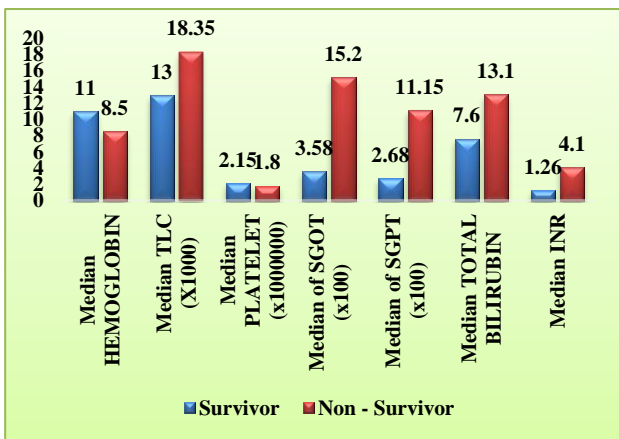


Figure 4: Maternal outcome.

This comparative analysis shows that poor maternal outcomes were seen with fall in the haemoglobin levels and platelet count, and with rise in the total leukocyte count, SGOT, SGPT, serum bilirubin levels, and INR.

Foetal outcome

There were total 117 deliveries, out of which there were total 85 live births, 30 still birth and 2 patients had spontaneous abortion. Out of the 85 live births there were total 46 full term deliveries and 39 preterm deliveries.

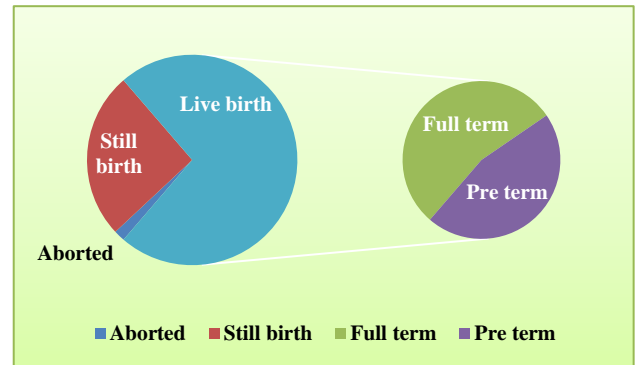


Figure 5: Foetal outcome.

Neonatal Intensive Care Unit admission and neonatal mortality

There were total 85 live births out of which 25 newborns required NICU admissions. Out of these 25 admissions, 19 babies were admitted for low birth weight and prematurity, while 5 had perinatal asphyxia, and one was admitted for evaluation of congenital cardiac anomaly. Out of these two infants one died because of prematurity and asphyxia, and the other because of extremely low birth weight and extreme prematurity.

DISCUSSION

Incidence

The incidence calculated in the present study is 3.09 per 1000 deliveries which are similar to the incidence in the study by Patra et al which is 3.95 per 1000 deliveries and lower than Kumar et al which are 8.6 per 1000 deliveries.^{7,8}

Age

Most of the affected patients in this study were between the ages of 21-30 years. Among them the most common age group affected is 21 to 25 years which constitutes 47.5% of the total affected individuals. These results are comparable with various other studies published which are shown in Table 9.

This result may suggest that younger age might have a greater predilection for hepatitis E infection.

Table 9: Majority of population affected.

Study	Majority of population affected	Percentage
Present study	21-25 years	47.5
Mishra S et al ⁹	21-24 years	41.90
Adjei A et al ¹⁰	21-25 years	46.15

Gestational age

The mean gestational age affected in the present study is 32.5 weeks of gestation with maximum number of patients in their third trimester. Comparison of this study with various other studies have been shown in the table below which shows higher number of pregnant women affected in the third trimester.

Table 10: Trimester distribution.

Study	Total pregnant hepatitis E patients studied	Percentage of patients in third trimester
Present study	120	87.50
Patra et al ⁷	132	88
Adjei et al ¹⁰	157	75.79
Badrakiya et al ¹¹	39	79.5
Shinde et al ¹²	52	63.4

Clinical presentation at the time of admission

In present study 92.5% of the patients presented with jaundice as their chief complaint, followed by fever which was seen in 41.6% of the affected cases, while 20.83% of patients had nausea/vomiting and 12.5% presented with altered sensorium. Yellowish discoloration of urine or sclera was observed in 91.42% of patients in the study published by Mishra et al conducted in the year 2016.⁹

According to Shinde et al almost all of cases in their study had nausea/vomiting, 86.5% had jaundice, 58% had fever, while 21.1% had hepatic encephalopathy.¹² Hence according to various studies that have been analyzed most of the affected patients have clinical jaundice and other common complaints are nausea or vomiting, fever while more critical patients have hepatic encephalopathy.

Type of labour

In present study total 117 patients delivered out of which most of the patients had a spontaneous labour and some underwent induction of labour. These results are consistent with the study conducted by Patra et al in which 41% of patients were in active labour on admission and 44% of patients went into active labour after admission.⁷ Therefore total 85% of the patients went into spontaneous labour. In the study by Badrakiya et al it was found that out of 39 patients studied with hepatitis E, 82% had spontaneous onset of labour.¹¹

Mode of delivery

Out of total 117 patients delivered nearly all patients delivered vaginally and only 15 patients underwent lower segment caesarean section. Majority of patients with hepatitis E had a spontaneous onset of labour, progressed well and delivered vaginally. In present study 87.1% patients had a vaginal delivery as compared to only 12.9% of lower segment caesarean section.

Similar results have been seen in a study conducted by Kumar et al at King George Medical College, Lucknow wherein 90.63% patients delivered vaginally and 9.37% underwent lower segment caesarean section.⁸ Also in the study by Badrakiya et al, 82% of pregnant patients with Hepatitis E had vaginal delivery while the percentage of caesarean section was 15.4%.¹¹ The inference from this analysis is that patients with hepatitis E go more often into spontaneous labour and deliver vaginally and less operative intervention is required. Moreover, authors have encountered situation where even though the pregnancy and foetus is precious, counselling for no operative intervention needs to be done from patient in maternal interest due to abnormal coagulation and deranged liver function tests. These abnormalities do increase the risk of poor maternal outcome if any operative intervention is done.

Maternal morbidity

Authors have analyzed maternal morbidity in terms of major medical complications occurring due to hepatitis E in pregnancy which is coagulation defect, hepatic encephalopathy, post-partum haemorrhage and hepatorenal derangements. In this study total 120 patients with hepatitis E were studied out of which nearly half of the patients had abnormal coagulation.

This result is slightly higher than the result obtained from Kumar et al in which 31.2% had abnormal coagulation; however, it is lower than the study published by Patra et al in which 79% of cases had coagulopathies due to Hepatitis E.^{7,8} The results of this present study are consistent with the studies published by Mishra et al and Badrakiya et al in which the percentage of patients with abnormal coagulation were 54.29% and 60% respectively.^{9,11}

Percentage of patients complicated with hepatic encephalopathy in this study was 28.3% which is found to be slightly higher to the studies published by Mishra et al, Kumar et al, and Badrakiya et al with their respective results as 20.95%, 21.8% and 15.4%.^{8,9,11}

Postpartum haemorrhage as a complication reported by Patra et al was 14% while according to present study it was 5% which is similar to as reported by Badrakiya et al.^{7,11} Hepatorenal complications were seen in very few patients which compares with Badrakiya et al where it was 2.6%.¹¹

Maternal mortality

In this present study there were total 24 maternal mortalities. Therefore, the percentage of maternal mortality in the present study is 20%. This result has been compared with various other similar studies. Patra et al shows it maternal mortality was approximately 15-20%.⁷ A paper published by Badrakiya et al shows that maternal mortality rate among the pregnant women with hepatitis E infection was 20.5% while Benita et al analyzed that maternal mortality rate in their study was 30-45%.⁹ Thus, hepatitis E infection is an important cause of maternal mortality.

Comparison of investigative parameters amongst the survivor group and the non-survivor group

In the present study it is found that the maternal outcomes were poorer with higher levels of SGOT, SGPT, S. Bilirubin, INR and total leukocyte count, and with falling levels of Haemoglobin and Platelet counts.

These results are consistent with the study published in Turkish Journal of Obstetrics and Gynaecology by Kumar et al.⁸ The average bilirubin level among the survivor group was 6mg/dl and non-survivor group was 15mg/dl which is consistent with the present study where it is 7.6mg/dl and 13mg/dl. The levels of SGOT and SGPT are also comparable where it was 313 IU and 332 IU in the survivors and 1240 IU and 1670 IU respectively amongst the non survivors in the study by Kumar et al to the results in the present study where the average levels of SGOT and SGPT in the patients discharged were 268 IU and 358 IU respectively and among the patients who died was 1115 IU and 1520 IU.⁸ The mean platelet count has also been compared in the both studies. In the study by Kumar et al it is 1.5 lacs in the survivors while 0.85 lacs in the non survivors while in this study it is 2.15 lacs in the survivor group and 1.8 among the non-survivor group.⁸ This data of present study has also been compared with the study published by Sahai S et al.¹³ In this study the average haemoglobin among the survivors was 7.6mg/dl and non survivors was 7mg/dl. In the study by Sahai S et al the average bilirubin, SGOT, SGPT and INR reported were 11.57mg%, 305.46 IU, 457.48IU, 1.12 amongst the survivors and 16.08mg%, 316.60IU, 310.69 IU, 2.40 amongst the non-survivors which were found to be similar with present study.¹³

Foetal outcome

In this recent study, out of 117 deliveries there were 85 live births, 30 still births and 2 spontaneous abortions. Among them nearly half were full term deliveries and remaining were preterm deliveries. The percentage of still birth was 25% and that of spontaneous abortion was only 1.72%. The neonatal intensive care unit admission was approximately 30%, in which majority were because of low birth weight and prematurity. The neonatal mortality rate among the babies admitted in NICU was 12%, and

the perinatal mortality rate was 28%. Kumar et al reports live birth rate of 56% and still birth rate of 45%.⁸ In the same study one third patients had term deliveries while the remaining majority were preterm deliveries. An article written by Patra et al says that in their study there were 21% live births and 54% still births.⁷ Out of which there were 90% preterm deliveries with 17% neonatal death. The rate of spontaneous abortion was 8% which is slightly higher than the present study. Similar study by Badrakiya et al shows 66% live births and 34% of still births.¹¹ There were total 25% full term deliveries and 72% preterm deliveries with neonatal intensive care unit admission rate of almost 70%. This data from various studies shows that there is higher incidence of still birth which ranges from one third to almost half of the deliveries with higher incidences of preterm deliveries ranging from nearly half to almost all the deliveries. The rate of spontaneous abortion is not increased probably due to lesser number of patients affected in their first trimester compared to the number of patients in their third trimester.

The limitations of this study were that actual number of the pregnant cases affected with hepatitis E is not obtained since this study is limited to a single tertiary care centre and only high-risk patient got transferred to the centre for further management.

CONCLUSION

The incidence of pregnant patients with hepatitis E in the present study is 3.09 per 1000 deliveries. It is found that nearly half of the patients which are diagnosed with hepatitis E were young and belonged to the age group of 21-25 years.

Maximum numbers of the patients when diagnosed were in their third trimester of pregnancy, showing that patients are more vulnerable for hepatitis E infection in their latter part of pregnancy. The most common presenting complaint of the patients in this study was jaundice or yellowish discoloration of sclera and urine which was found in almost 90% of the cases, followed by fever, nausea/vomiting and altered sensorium.

Almost 80% of the cases went into spontaneous labour, either before or after admission and rest had to be induced mainly in view of intrauterine foetal demise or preterm premature rupture of membranes. Majority of the patients delivered vaginally and only 13% of the patients had to be operated. In this study approximately 51% of the patients were morbid out of which 38% could not survive.

The maternal mortality rate in the present study is found to be 20%. Higher mortality was found in patients with hepatic encephalopathy and disseminated intravascular coagulation. The maternal outcome was poorer with rising levels of SGOT, SGPT, bilirubin, INR. There were higher percentage of still birth and increased incidence of

preterm deliveries with poor perinatal outcome in patients suffering from hepatitis E, especially in their third trimester.

Early diagnosis and rapid management of the complications such as correction of abnormal coagulation and supportive management is the only treatment available at present. ICU admission and with strict maternal and foetal monitoring can help improve the outcome.

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