Fetomaternal Outcome of Pregnancy with Hepatitis E Infection

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ABSTRACT

Background and Objective*: Hepatitis E viral infection is one of the major health concerns in the pregnant women owing to its fulminant nature in pregnancy and contribution to increase the mortality in pregnant women as compared to non-pregnant females. So, this study was conducted with an objective to find out the pregnancy related mortality, maternal morbidity and fetal outcome suffering with hepatitis E (HEV) in pregnancy.*

Methods: *This study was conducted in Hussain Memorial Hospital Lahore and Sir Ganga Ram Hospital, Lahore for the period of one year and seven months between May 2017 and November 2018. This cross sectional study recruited 60 females with serologically proven HEV in pregnancy. All of these targeted patients were admitted in the aforesaid hospital and followed with coagulation profile and liver function test. The record of maternal mortality, morbidity and fetal outcome was duly maintained.*

Results: *More maternal morbidity was noted in patients who were admitted in the third trimester with clinical disease and based on laboratory results i.e. the derangement of haematological and biochemical tests. Of the 60 targeted patients, majority of the patients (73.33%) were discharged home safely, therefore, remaining patients were expired with the overall mortality rate of 26.67%. Moreover, perinatal mortality rate was recorded as 30.3 per 1000 live birth.*

Conclusion: *In conclusion, Hepatitis E is a serious issue in underdeveloped and developing countries with high maternal morbidity and mortality rates in pregnancy especially last trimester. It also increases the risk of perinatal mortality, morbidity and preterm delivery.*

KEYWORDS*: Perinatal mortality, Liver failure, Acute, Hepatitis E virus, Maternal mortality.*

INTRODUCTION

Hepatitis is one of the major challenging conditions in pregnancy for the obstetrician. In Pakistan, all types of hepatitis are endemic, moreover, both sporadic as well as epidemic forms have been reported. Viral hepatitis (i.e. hepatitis A and E) caused by five viruses which are basically waterborne agents. Most of the time, this infection acquired by drinking faecal contaminated water.[1] Pakistan is a developing country with generally low socio-economic and poor hygienic condition.[2] Hepatitis E is also an enterically transmitted infection and occurs in epidemics commonly in South East Asia, Africa other developing countries than American and European countries.[1] Infection occurs in epidemics during summer and rainy seasons.[3] It is self-limiting illness having good prognosis except in pregnant women where mortality rate can reach upto 20%. Transmission of HEV from mother to fetus and through transfusion of HEV infected blood has been shown to occur.[4,5]

It is observed that high levels of steroid hormones are associated with pregnancy. Moreover, viral replication may be promoted by these steroid hormones. Also, Hepatic cells directly inhibited them, which may predispose to hepatic dysfunction and failure when exposed to infectious pathogens. Steroid hormones are immunosuppressive, the immunological changes include down regulation of p65 component of NFkB with a predominant Th2bias in the T-cell response along with host susceptibility factors mediated by HLA expression.[6]

Globally, a viral hepatitis in pregnancy has been a subject of continuous controversy and interest as both the 'severity' and 'incidence' vary widely in pregnancy. The incidence and severity in pregnancy is reported as low as 1 in 20,000 in North America and Western Europe, whereas, in outbreaks of waterborne Hepatitis E in India and Asia, the case fatality rate is 1–2% and up to 10–20% in pregnant women.[7] With hepatitis, fulminant hepatic failure is more common in pregnant women with fatality rate of 30%.[8] Reasons for the

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difference remain unclear in geographically different areas regarding the outcome of HEV but could also be the result of 'early childhood HEV exposures', 'modify subsequent responses to exposure to the virus' and 'produce long-lasting immunity'. On the other hand, the predominant HEV genotype in some geographical location could be less virulent than those in others.[7]

This study was conducted to determine the frequency of Hepatitis E in pregnancy, its clinical representation, maternal mortality, morbidity and perinatal outcome.

METHODS

After obtaining approvals from institutional review board of ethical the study was carried out in the private and public hospital situated in Lahore, the provincial capital of Punjab i.e. Hussain Memorial Hospital Lahore and Sir Ganga Ram Hospital Lahore for the period of one year and seven months between May 2017 to November 2018, respectively. The pregnant women either booked or unbooked with serologically proven HEV alone were admitted and included in the study. All patients having hepatitis A, B, C other than hepatitis HEV were excluded from the study. Diagnosis was made on clinical presentation i.e. jaundice, vomiting, loss of appetite, altered sensorium, baseline investigations i.e. prothrombin time, liver function test and complete blood count,serological and APTT tests including anti-HEV, anti-HAV, anti-HCV and HBsAg. All these patients were followed up during the stay in the hospital regarding their pregnancy status either continued or terminated, mode of termination and either induced or spontaneous onset of labour. Any complication including obstetrical, medical and surgical were noted. Maternal and foetal morbidity was recorded and maternal mortality and was also calculated.

STATISTICAL ANALYSIS

Data were analyzed using Statistical Package for Social Sciences (SPSS version 22) and descriptive statistics were rendered to achieve the objective of the study.

RESULTS

Total of 60 patients were admitted in the hospital with age ranged between aged 22 to 40 years (Fig.1). Table-1 showed that patients presented at different gestational ages with maximum during 3rd trimester and postpartum period. Termination of pregnancy was done according to the gestational age. Further information was depicted in (Fig:2. and Table-2). All patients presented with yellowish discoloration of sclera and generalized weakness. Out of the 60 patients, 33.3% patients presented with altered sensorium and vomiting each. Moreover, 66.6% patients were with loss of appetite, 16.6% with upper abdominal pain, 10% with preterm labour pains and 3.33% with generalized itching. Majority of the patients 36 (60%) required ICU care. Of the 60 targeted patients, majority (73.33%) were discharged home safely, therefore, remaining patients were expired with the overall mortality rate of 26.67% (Table-2). Among 60 pregnancies, 34 babies delivered alive and healthy, 6 neonates were managed conservatively and the perinatal mortality was 33.3%. All these patients were serologically proven Hepatitis E positive. Haemoglobin of these patients was between 6-12 g/dl with mean value of 9.33 ± 1.5 g/dl. Platelets ranged between 30 – 306 × 10^9/L with mean of 157 ± 82.4 × 10^9/L. Prothrombin time was between 10 – 93 seconds with mean volume of 28.57 ± 24.9 seconds, APTT ranged between 22 – 120 seconds with mean volume of 44.67 ± 24.3 seconds. Serum bilirubin of these patients varied between 1 – 49 mg/dl with mean of 13.83 ± 11.62 mg/dl, SGPT ranged from 24 – 1933 IU/L with mean value of 602 IU/L. Maxi-mum derangement of haematological and biochemical

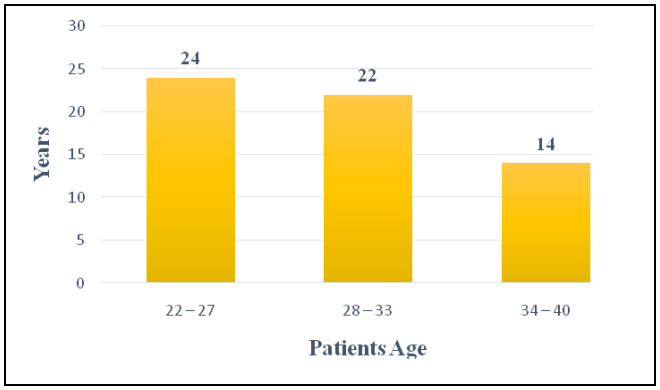

Fig. 1: *Patients age (years) (N = 60).*

Table- 1: *Gestational age (in weeks) (N = 60).*

Gestational age	*Frequency*	*Percentages (%)*
0 – 12	4	6.67
13 – 26	10	16.67
27 – 40	30	50.00
Postpartum	16	26.67

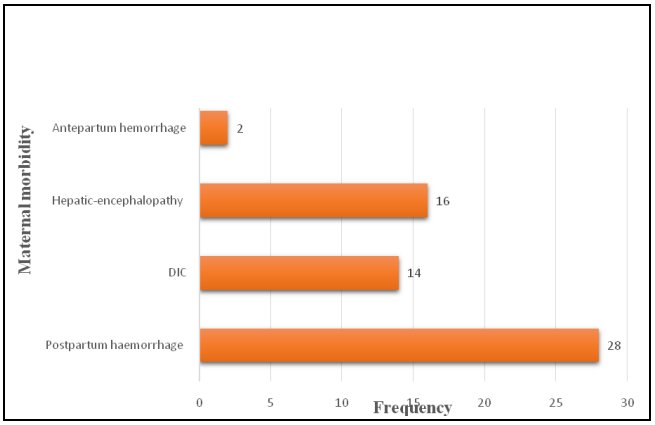

Fig. 2: *Fetomaternal Outcome - Maternal Morbidity (N = 60).*

tests was noted in patients who presented during third trimester and postpartum.

Table- 2: *Fetomaternal Outcome (N = 60).*

Morbidity	*Frequency*	*Percentages*
Maternal Outcome		
Recovered	44	73.33
Maternal Mortalities	16	26.67
Total	60	100.00
Mode of Termination of Pregnancy		
Induction of labour (followed by SVD)	6	10.00
Preterm SVD	38	63.33
Lower segment c/section	6	10.00
Hysterotomy	4	6.67
Conservative management	6	10.00
Total	60	100.00
Fetal Outcome		
Alive / healthy	34	56.67
Intrauterine deaths	8	13.33
Neonatal deaths	10	16.67
ERCP done	2	3.33
Conservative management	6	10.00
Total	60	100.00

DISCUSSION

HEV is one of the hepeviridae family viruses which is a single-stranded RNA.[9] Hepatitis E is also one of the emerging infectious diseases of great global importance.[10] In several countries, this issue refers to the major public health concern where safe drinking water is a serious problem. Most frequently, HEV infection occurs in rainy season. Mainly, this disease is prevalent among young adults whose age ranged between 15 to 40 years which is also in accordance with this study as 70% patients were between the age of 22 – 30 years and 30% were between 31 – 40 years. During epidemics, the course of disease has increased severity and incidence in pregnant women.[11]

Kumar et al.[12] observed that two-third of the pregnant women with HEV had preterm deliveries which is consistent with our results in patients (66.6%) had preterm deliveries between 25 – 35 weeks of gestation. Patients whose pregnancies were terminated earlier irrespective of gestational age had better maternal outcome.

Fifty percent patients presented during the third trimester and maximum morbidities were noted in this group, which is consistent with the study of Jaiswal et al.[13] where 50 and 51% HEV infected pregnant females developed fulminant hepatic failure during second and third trimester, respectively, in comparison to 16.66% females developing during the first trimester. This shows increasing incidence of fulminant hepatic failure with increasing gestational age.

Begum et al.[14] reported that HEV was more prevalent in the third trimester of pregnancy (30.3%) than the second trimester (25.0%). This is consistent with the study as 33.3% patients presented in third trimester and 20.0% in second trimester. This could be termed as a potential disaster for mother as well as child.

During pregnancy, HEV infection is termed as fatal and fulminant, specifically, if it occurs in the third trimester. During the second trimester, the mortality rate is approximately 20.0% which increases up to 45.0% in the third trimester which is consistent with the present study in which maternal mortality was 29.3% and 30.3% perinatal mortality rate and all mortalities noted were between third trimester and postpartum period.[10]

Kumar et al.[12] reported that the mortality rate was 26.6% among HEV positive pregnant women. Moreover, vertical transmission was observed in 33.3% and had severe forms of hepatitis in the third trimester of pregnancy; hepatitis E in pregnancy is associated with mortality and high rates of preterm labour. Begum et al.[14] reported 22.2% fatality rate with maximum severity during 3rd trimester 44.4% which is comparable with this study.

In New Delhi, Petra and colleagues confirmed maternal mortality rate ranged from 15 – 20% in pregnant women with HEV.[15] However, 30% mortality rate as compared to 1% in the general population was reported by Nassim et al.[16] In an Indian study conducted in Mumbai, Banait et al.[17] reported perinatal mortality (69%) and maternal mortality (54%) was high in pregnant women with HEV which is also much higher than the results of our study. Another study confirmed that mortality rate ranged from 30 – 45% and in some cases may be exceeded as high as 70%.[18] Among pregnant patients with HEV, 20% mortality rate was reported by Saeedi et al.[19] Therefore, in a Pakistani study, Aliya and colleagues reported 14 – 25% mortality rate and 30% perinatal mortality rate in patients with HEV in pregnancy, especially during 3rd trimester. Ahmed reported 25% maternal mortality rate and 17.8% intrauterine deaths in pregnant HEV positive mothers.[20] Shukla reported 33.3% maternal mortality rate in patients with hepatitis E in pregnancy.[21] The main limitation of this study was its small sample size.

CONCLUSION

Hepatitis E is a serious issue in underdeveloped and developing countries with high maternal morbidity and mortality rates in pregnancy especially last trimester. It also increases the risk of perinatal mortality, morbidity and preterm delivery.

LIMITATIONS OF STUDY

The above mentioned problem needs to be focused and more studies with large sample size should be made to find ways to improve the prognosis.

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AUTHOR'S CONTRIBUTION
AT, HMD and NM: Collect data, Manuscript writing, analysis of data and approve the final draft of the manuscript.
SW, GER and AS: Conception, analysis of data, manuscript writing, approval of the final draft.

CONFLICT OF INTEREST
None to declare.

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