

# Outcome of Hepatitis-E Virus Infection among Pregnant Women Admitted in a Tertiary Care Hospital

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## Author's Contribution

<sup>1</sup> Conception of study

<sup>2</sup> Experimentation/Study conduction

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## Article Processing

Received: 17/01/2022

Accepted: 05/04/2022

**Cite this Article:** Wasim, T., Mushtaq, J., Wasim, M. Outcome of Hepatitis-E Virus Infection among Pregnant Women Admitted in a Tertiary Care Hospital. *Journal of Rawalpindi Medical College*. 30 Jun. 2022; 26(2): 306-310.  
DOI: <https://doi.org/10.37939/jrmmc.v26i2.1882>

**Conflict of Interest:** Nil

**Funding Source:** Nil

**Access Online:**



## Abstract

**Objective:** To evaluate hepatitis E infection outcomes among pregnant women admitted to a tertiary care hospital.

**Materials & Methods:**

**Study Design:** Cross-sectional study

**Study Setting:** Department of Gynecology and Obstetrics Unit I, Services Institute of Medical Sciences, Lahore

**Study Duration:** May 2019 to Feb 2020, after approval from Institutional Review Board.

**Data Collection Procedure:** 30 Pregnant women with Hepatitis E confirmed on ELISA IgM, fulfilling the inclusion criteria age, 25 - 40 years of age in any trimester of pregnancy will be included in the study through Non-probability/convenience sampling. Data was entered and analyzed in SPSS ver: 25.0 Qualitative variables like Socio-demographic details and Clinical variables like the fetomaternal outcome were presented as frequency and percentages. The outcome was cross-tabulated with a demographic and clinical profile. The Chi-square test was applied with  $p < 0.05$  and was taken as statistically significant.

**Results:** 30 patients were recruited for the study. 96.7% were between the age of 18 - 40 years. 43.3% were primigravida. 76.7% were delivered through spontaneous vaginal delivery. 66.7% had coagulation defects, Fetal outcomes showed 63.3% were alive, 20.0% were stillbirth and 16.7% had ENND. The maternal outcome was 96.7% recovered from Hepatitis E. 14.3% of pregnant women who were delivered with LSCS died which was statistically significant. ( $p=.045$ )

**Conclusions:** The present findings suggest a high Hepatitis E infectivity in pregnancy results in considerable high maternal and fetal morbidity and mortality. This high disease burden can be minimized by the provision of clean drinking water and access to better sanitary conditions for pregnant women.

**Keywords:** HEV, Hepatitis E infection, HEV infection, Pregnancy.

## Introduction

Hepatitis E virus (HEV) infection in developing countries is one of the main reason of morbidity and mortality among pregnant women and there are disproportionate mortality rates in low-income and developing countries among pregnant women.<sup>1</sup> Hepatitis E infection among pregnant women poses a great challenge for the obstetrician due to severe pregnancy-related complications including Maternal complications like preterm labour, preterm premature rupture of membrane (PPROM), antepartum hemorrhage (APH), postpartum hemorrhage (PPH), and maternal coagulopathy and Fetal complications like meconium stained liquor and intrauterine fetal death.<sup>2</sup>

The situation of the Hepatitis E virus (HEV) in Pakistan is endemic in nature although most cases among young adults are asymptomatic. But Hepatitis E infection becomes fatal in pregnancy and there is substantial maternal and fetal morbidity and mortality.<sup>3</sup>

The Hepatitis E vaccine trials have been successfully conducted in the southern Asian population and results have been very promising, results have shown that the candidate vaccines are very effective and well-tolerated but the availability of these vaccines to susceptible populations has still not been accessible to populations.<sup>4</sup>

In a study done by Parsad et al, they recruited pregnant women who were anti-HEV IgM-positive and were symptomatic to evaluate maternal and fetal outcomes in these pregnancies, 5.0% of women died due to complications, among fetal complications 11.0% had PROM, 80.0% had prematurity and one antenatal death with the rate of vertical transmission of 28.0%. This high maternal morbidity and mortality among the Asian population warrant a need for further studies of virus genotyping and its infectivity and virulence.<sup>5</sup>

The data collected during 2001-2007 surveillance of more than 110,000 pregnancies among 650,000 women in rural Bangladesh showed 9.8% of pregnancy-related deaths due to acute hepatitis and the majority of these deaths were attributed to hepatitis E. The findings of this and other similar studies show that as many as 10,500 maternal deaths each year are mainly due to HEV infection during pregnancy and can be prevented by the use of HEV vaccines.<sup>1,6,7</sup>

HEV infection among pregnant women is very prevalent in low and middle-income countries mainly due to very limited access to clean potable water, poor sanitation, hygienic condition, and limited access to

health services.<sup>8,9</sup> HEV infection among these pregnant women occurs both as sporadic cases and seasonal outbreaks in these areas. These outbreaks' main reason is fecal contamination of drinking water supplies and usually, several hundred to several thousand persons are affected. Also, some of these outbreaks are more prevalent in areas where there are humanitarian emergencies like a refugee situation, internally displaced persons, or areas of war zones, where clean and safe water supply is difficult and challenging.<sup>10</sup>

Objective: To evaluate hepatitis E infection outcomes among pregnant women admitted to a tertiary care hospital.

## Materials and Methods

A Cross-sectional study was conducted at the Department of Gynaecology and Obstetrics Unit I, Services Institute of Medical Sciences, Lahore from May 2019 to Feb 2020. After approval from Institutional Review Board. A sample size of 30 was calculated using the WHO calculator that uses formulae i.e.  $n = (z)^2 p (1 - p) / d^2$  using a 95% confidence interval with an 8% margin of error assuming 5% mortality among pregnant women with hepatitis E from the study of Parsad et al. Pregnant women with Hepatitis E confirmed using IgM antibody by ELISA among those fulfilling the inclusion criteria of age between 25 - 40 years of age in any trimester of pregnancy will be included in the study through Non-probability/convenience sampling. Pregnant women with hepatitis E and pre-existing conditions like heart diseases and malignancies will be excluded. A detailed demographic history was taken along with complications during pregnancy, obstetric complications due to hepatitis E like antepartum or postpartum hemorrhage, preterm premature rupture of membranes, meconium stained liquor, maternal coagulopathy, and intrauterine death was observed. Delivered babies are followed up to 1 week postpartum to determine the perinatal outcome in form of admission, vertical transmission to baby, cause of ENND, or alive baby. Pregnant women with hepatitis other than hepatitis E, drug-induced hepatitis, cholestasis, jaundice of pregnancy, and acute fatty liver of pregnancy were excluded. SPSS version 25.0 was used for data analysis. Mean and Standard deviation was calculated for variables like age, disease duration, and frequency, and percentages were calculated for variables like Socio-demographic and feto-maternal outcome. Chi-square test was applied to

assess statistical significance for the fetomaternal outcome and demographic variable with  $p < 0.05$  was taken as statistical significant.

### Results

30 patients were recruited for the study. 96.7% were between the ages of 18-40 years. 43.3% were primigravida. 96.7% were between 27-40 weeks of pregnancy. 53.3% were living in an urban area and 40.0% were from urban slum areas. 76.7% of our respondents were educated having secondary and post-secondary education. 83.3% presented with yellow discoloration of the body, sclera, and itching. (Table 1)

**Table 1: Demographic profile of subjects**

Variables n=30		Frequency	Percentage
Age	<18	1	3.3
	18-40	29	96.7
Parity	primigravida	13	43.3
	multigravida	17	56.7
DOP	13-26 weeks	1	3.3
	27-40 weeks	29	96.7
Residential area	urban	16	53.3
	urban slum	12	40.0
	Rural	2	6.7

Education	illiterate/elementary	1	3.3
	matric/F.A	23	76.7
	Graduation/above	6	20.0
Occupation	Housewife	30	100.0
	Working	0	0.0
Presenting complaint	Yellow discoloration of the body and itching	25	83.3
	Fever	1	3.3
	Nausea vomiting loss of appetite	1	3.3
	Decreased fetal movements	3	10.0

Clinical profile of subject shows 76.7% were delivered through spontaneous vaginal delivery. Maternal complications showed that 66.7% had coagulation defects, 30.0% developed hepatic encephalopathy, and 3.3% developed fulminant hepatic failure. Obstetric complications showed that 50.0% had a preterm delivery, 20.0% developed PPH, and IUGR was present among 26.7% of pregnancies. The fetal outcome showed that 63.3% were alive, 20.0% were stillbirth and 16.7% had ENND. The maternal outcome was 96.7% recovered from Hepatitis E. (Table 2)

**Table 2: Socio-demographic profile and maternal outcome Cross-tabulation**

		Maternal outcome				P value
		Recovered		Death		
		Frequency	Percentage	Frequency	Percentage	
Age	<18 years	1	100.0	0	0.0	.850
	18-40 years	28	96.6	1	3.4	
Parity	Primigravida	13	100.0	0	0.0	.374
	multigravida	16	94.1	1	5.9	
Residential area	urban	16	100.0	0	0.0	.460
	urban slum	11	91.7	1	8.3	
	Rural	2	100.0	0	0.0	
Education	illiterate/elementary	1	100.0	0	0.0	.315
	matric/F.A	22	95.7	1	4.3	
	Graduation/above	6	100.0	0	0.0	
Mode of delivery	SVD	23	100.0	0	0.0	.045
	LSCS	6	85.7	1	14.3	

The outcome was cross-tabulated with demographic and clinical characteristics. The death occurred in 3.4% of pregnant women 18-40 years. ( $p=.850$ ) and 5.9% of multigravida women ( $p=.374$ ). 8.3% of deaths were in urban slum areas. ( $p=.460$ ) and 4.3% of pregnant women who were educated. ( $p=.315$ ). 14.3% of pregnant women who were delivered with LSCS died

because of fulminant hepatic failure which was statistically significant. ( $p=.045$ ). (Table 3)

**Table 3: Clinical profile of subjects**

Variables n=30		Frequency	Percentage
Mode of delivery	SVD	23	76.7
	LSCS	7	23.3

Maternal complications	Coagulation defect	20	66.7
	hepatic encephalopathy	9	30.0
	fulminant hepatic failure	1	3.3
	Obstetric complications		
Obstetric complications	PPROM	1	3.3
	Preterm birth	15	50.0
	PPH	6	20.0
	IUGR	8	26.7
Maternal outcome	Recovered	29	96.7
	Death	1	3.3
Fetal outcome	Alive healthy	19	63.3
	stillbirth	6	20.0
	ENND	5	16.7

## Discussion

A very high burden of HEV infection is seen among pregnant women, especially in developing countries in recent years. Infection with hepatitis E virus during pregnancy is usually associated with poor foeto-maternal outcomes with a two to three-fold increase in intrauterine fetal death, a three-fold increase in poor intrauterine fetal maturity, and a significant increase in the likelihood of maternal deaths. Global Burden of Disease<sup>8,9</sup> in several studies have estimated the HEV seroprevalence among women of childbearing age (15 to 45 years) to be 5-22% and a high IgM seroprevalence of more than half of HEV infection among symptomatic women depicts an endemic situation of HEV is endemic in these regions.<sup>11-17</sup>

In our study among pregnant females, 43% were primigravida, and 56% were multigravida. Among these pregnant women, 96.7% were in the third trimester of pregnancy these findings are similar to previous studies where the incidence of HEV infection increases with increased gestational age, and the relation between HEV infection and gravid uterus was not evaluated in previous studies.<sup>8,9-11</sup>

Singh et al researchers analyzed the rate of HEV infection among pregnant Indian women who were admitted to tertiary care hospitals. A high positivity rate of 40.0% for IgM anti HEV was seen. Other study findings suggest similar findings in contrast with other studies evaluating the burden of disease where a high burden of HEV infection among pregnant women presenting in tertiary care hospitals who were living in high endemic areas where maternal and fetal outcomes are poor and a high rate of vertical transmission.<sup>11-15</sup>

Singh et al study also depicted that 76.7% of women had a spontaneous vaginal delivery and among them,

52.0% had in the second trimester among pregnancies in the third trimester 50% had a fulminant hepatic failure, also no statistically significant association was found in fatality rates and HEV infected pregnant women who presented between the second and third trimesters (66.6% vs. 71.43%) respectively.<sup>11</sup>

In our study maternal complications showed that 66.7% had coagulation defects, 30.0% developed hepatic encephalopathy, and 3.3% developed fulminant hepatic failure. Obstetric complications showed that 50.0% had a preterm delivery, 20.0% developed PPH, and IUGR was present among 26.7% of pregnancies. The fetal outcome showed that 63.3% were alive, 20.0% were stillbirth and 16.7% had ENND.

In a study by Parsad et al<sup>5</sup> maternal mortality was evaluated among pregnant women with HEV infection and 5.0% of women died including one antenatal death. 80.0% of the newborn were premature and PROM was present in 11.0% and were the commonest fetal complications noted. The vertical transmission rate of HEV infection in this study was 28.0%. In our study maternal outcome was 96.7% who recovered from Hepatitis E and the fetal outcome showed 63.3% were alive, 20.0% were stillbirth and 16.7% had ENND consistent with Parsad et al study.<sup>5</sup> Similar foeto-maternal outcomes and risk factor prevalence have been reported by Solanki, Sahi, and Obiri-Yeboah et al studies.<sup>20-22</sup>

Kumar et al study findings are also consistent with our study findings. The researcher included 32 anti-HEV immunoglobulins M-positive pregnant women who were analyzed for foeto-maternal outcomes. The most common fetal complications were intrauterine demise with prematurity and among maternal outcome maternal mortality and premature rupture of membranes was the frequency and there was a statistically significant association with Hepatitis E infection.<sup>23</sup> Similarly study Helema et al conducted to determine the frequency of Hepatitis E in pregnancy, its clinical presentation, maternal morbidity, mortality and perinatal outcome. the maternal mortality rate of 29.3% and the rest were discharged safely. The perinatal mortality rate was 30.3 per 1000 live births. Our study findings also reflect high foeto-maternal complications.<sup>24</sup>

## Conclusion

Our study findings suggest that Hepatitis E infectivity among pregnancy with high foeto-maternal morbidity and mortality among pregnant women among women

presenting in tertiary care hospitals. The burden of HEV infection among these pregnant women can be reduced by preventive measures like the provision of a safe water supply and a better sanitary environment for pregnant women.

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