

## Outcomes of Hepatitis E in Pregnancy

IRAM INAM<sup>1</sup>, GHIAS UL HASSAN<sup>2</sup>, SABOOHI SAEED<sup>3</sup>, SAADIA SAJJAD<sup>4</sup>, SAIMA SHEIKH<sup>5</sup>

<sup>1</sup>Associate Professor, Department of Gynae/Obs, Continental Medical College Lahore, Pakistan

<sup>2</sup>Assistant Professor, Department of Gastroenterology, PGM/LGH Lahore, Pakistan

<sup>3</sup>Professor & Head of Department Physiology, Azra Naheed Medical & Dental College Lahore

<sup>4</sup>Associate Professor Department Physiology, Abu Ammara Medical & Dental College Lahore

<sup>5</sup>Assistant Professor Department Physiology, Khawaja Safdar Medical College Sialkot

Correspondence to: Iram Inam, Email: [ahnmalik@hotmail.com](mailto:ahnmalik@hotmail.com), Cell: 0322-5930030

### ABSTRACT

**Introduction:** Hepatitis E virus infection is an emerging challenge of the developing world. During pregnancy, hepatitis E Virus results in devastating effects endangering the life of both mother and fetus. Hepatitis E contribute to 19% to 25% of maternal and 7-13% of all neonatal deaths. Purpose of this study is to see the association between hepatitis E virus infection and fetomaternal outcomes in pregnancy.

**Material & Methods:** A prospective study design was used. Study was conducted in a tertiary health care sector for a period of March 2018 to January 2021 with sample size of 60 pregnant women. Study was conducted after getting institutional approval and informed consent was taken from all the study participants. Ethical considerations were followed throughout the study period. Data was analyzed using SPSS version 23.0 and descriptive statistics was used.

**Results:** Out of 60 pregnancies, 19 (30%) suffered with PPH, 14 (23.33%) had history of DIC and 16 (26.66%) cases of hepatic encephalopathy were evident. Preterm SVD was a majority reason seen for ending the pregnancy. Results showed that hepatitis E virus caused multiple fetal morbidities.

**Conclusion:** High mortality rate was evident in hepatitis E virus infection affected pregnancies in this study. There is a need to educate pregnant ladies regarding preventive measures to avoid fulminant consequences. Emphasis should be given to follow hygienic practices during pregnancy and proper antenatal visits are mandatory to educate the women.

**Keywords:** Hepatitis E, Fetus Outcomes, Pregnancy, Maternal.

### INTRODUCTION

Hepatitis E virus poses a huge threat during pregnancy resulting in unforeseen circumstances. Hepatitis E virus infection is an emerging challenge of the developing world<sup>1</sup>. In pregnancy, Hepatitis E virus casts most devastating effects endangering the life of both mother and fetus. Many other hepatitis viruses also cause complications during a pregnancy by targeting the mother and fetus<sup>2</sup>. Globally, all types of hepatotropic viruses prevail in pregnancy as it's a risky period of life. In developing countries like Pakistan, all types of hepatic viruses persist that are responsible for acute hepatitis. Hepatitis viruses remain endemic in all areas of Pakistan both in sporadic and epidemic forms<sup>3</sup>.

Considering all the other types of viral hepatitis, A & E hepatitis are water borne diseases that are transmitted through feco-oral route by drinking contaminated water. Un-hygienic lifestyle habits are risk factor for promoting hepatitis E infection<sup>4</sup>. The incubation period of hepatitis E virus is 8-10 weeks and infection normally resolves in 6 weeks without any chronic consequences. In Pakistan, owing to low socioeconomic status and poor living conditions, chances of acquiring hepatitis E virus infection are high especially in pregnancy<sup>5</sup>. Cases of hepatitis E are mostly reported during summer season as it spread as an outbreak. Hepatitis E cases are diagnosed and cured early except in pregnancy where the effect are more overwhelming leading to high mortality rate<sup>6</sup>.

There are no chances of getting Hepatitis E virus infection from person to person contact. Although risk of transmission from mother to fetus and through contaminated blood are reported. In 1950, this disease was first explored in Indian regions in sporadic form<sup>7</sup>. Pregnancy period is associated with intake of steroidal hormones, so these steroids enhance viral replication in human body and cause deteriorating circumstances. Viral hepatitis E forecast a threatening hepatic effects leading to liver dysfunction and failure in several cases during pregnancy through viral overload resulting from steroid ingestion<sup>8</sup>. Steroids are involved in suppressing the human immunity and in pregnancy the immunosuppressive effects of steroidal hormones cause down regulation of P<sub>65</sub> component of NFκB along with host susceptibility effects through the mediation of HLA expression. Effects of hepatitis E virus infection vary in different parts of the world both in incidence and severity<sup>9</sup>.

In Western countries, risk of Hepatitis E virus infection are low compared to Eastern countries. Reasons for this geographical distribution of hepatitis E Virus infection remained a subject of controversy<sup>10</sup>. Immune responses in West regions may present as a protection against infection. During pregnancy hepatitis E Virus results in fulminant hepatic failure. Chances of getting fulminant infection are rare in non-pregnant population<sup>11</sup>. Viral Hepatitis E mostly affects 2<sup>nd</sup> and 3<sup>rd</sup> trimester of pregnancy leading to obstetric complications like PROM, PPH, spontaneous abortions and IUFD etc. E Virus also casts hostile effects on fetus resulting in prematurity and low birth weight babies<sup>12</sup>.

Evidences suggested the facts that hepatitis E virus infection in pregnancy contribute towards 19% to 25% of maternal and 7-13% of all neonatal deaths<sup>13</sup>. Also 58% deaths were ascribed to liver failure associated with hepatitis E virus infection in pregnant ladies<sup>14</sup>. Effects of hepatitis E virus vary in pregnancies and cause multiple fetomaternal outcomes. Research provides information regarding hepatitis E virus infection in pregnancy but effect of virus on different maternal and fetal outcomes remained a subject of controversy<sup>15</sup>. Therefore, this study is undertaken to see the association between hepatitis E virus infection and fetomaternal outcomes in pregnancy.

### METHODOLOGY

A prospective study design was used to assess the effects of viral hepatitis E infection on fetomaternal outcomes. Study was conducted in a tertiary health care sector for a period of March 2018 to January 2021. A total of 60 pregnant women having positive HEV infection confirmed with clinical presentation and serological testing were included in this study. Women with other types of viral hepatitis i.e A, B, C & D were excluded from this study. 60 pregnant women with confirmed HEV infection were followed during the defined study period in tertiary health care sector. Outcome variables were maternal and fetal morbidity and mortality. During the study period, pregnant ladies were assessed for any pregnancy related complications like termination of pregnancy, any spontaneous abortion, PROM, early labour, IUFD, IUGR, PPH, maternal and fetal mortality etc.

Study was conducted after getting institutional approval and informed consent was taken from all the study participants. Ethical considerations were followed throughout the study period. Confidentiality of data was maintained and rights of participant

were reserved. Data was analyzed using SPSS version 23.0 and descriptive statistics was used to display the data in the form of frequency and percentages.

## RESULTS

A total of 60 pregnant women participated in this study. Demographics of the participants are shown in table#1.

Table 1: Demographics of the Study Participants.

Characteristics	Frequency	Percentage
Age of Participants in Years		
22-27	24	40%
28-33	22	37%
34-40	14	23%
Gestational age		
0-12	4	6.67%
13-26	6	10%
27-40	30	50%
Postpartum	20	33.33%
Yellowish discoloration of sclera	60	100%
Generalized weakness	21	35%
Altered sensorium	20	33.33%
Loss of appetite	44	73%
Preterm labour pain	6	10%

Above mentioned table shows that mostly participants belong to age group 22-27 years. Gestational age of mother shows that most women were in their 3rd trimester of pregnancy. All the studied women had yellowish discoloration of sclera. Demographics of participant showed that generalized weakness was present in 21 pregnant women out of 60. Also, table#1 shows that 20 women had altered sensorium, 44 having loss of appetite and 6 women presented with preterm labour pain.

Table 2: Maternal outcomes of HEV Infection in Pregnancy.

Maternal Morbidity	Frequency	Percentage
Postpartum Hemorrhage	19	30.00%
DIC	14	23.33%
Hepatic Encephalopathy	16	26.66%

Above mentioned table clearly depicts the data of mother's morbidity corresponding to hepatitis E infection during pregnancy. Out of 60 pregnant women, 19 (30%) women suffered with PPH, 14 (23.33%) had history of DIC and 16 (26.66%) cases of hepatic encephalopathy were evident as in table #2.

Table 3: Mode of pregnancy termination due to hepatitis E virus infection.

Mode of Termination	Frequency	Percentage
Induction of Labour	07	11.66%
Preterm SVD	38	63.33%
C-Section	06	10.00%
Hysterectomy	01	1.66%
D & E	02	3.33%
Conservative Management	06	10.00%

Results of this study show that induction of labour was done in 10% cases. Preterm SVD was a majority reason seen for ending the pregnancy. C-section done in 10% cases while conservative management was underwent in 06 cases out of 60 shown in above mentioned table.

Table 4: Fetal outcomes of hepatitis E in pregnancy.

Fetal Outcomes	Frequency	Percentage
Alive/healthy	34	56.67%
IUD	8	13.33%
Neonatal deaths	10	16.66%
ERCP done	2	3.33%
Conservative Management	6	10.00%

Results related to fetus outcomes are shown in table #4. Out of 60 pregnancies, 34 delivered normal and healthy babies. Also, 8 cases of IUD and 10 presented with neonatal death. ERCP was done in 2 while conservative management done in 6 babies.

## DISCUSSION

Hepatitis E is a disease of youngsters and mainly affects individuals in the age of 20-30 years. In this study, results show that mostly individuals affected with hepatitis E infection belong to age group 22-27 years. Other studies also show similar results<sup>16</sup>. Present study also suggest that hepatitis E infection mostly affects pregnant women in 3<sup>rd</sup> trimester. Findings show that in the third trimester of pregnancy, 50 % cases affected hepatitis E infection. These results were consistent with other studies having majority cases in the last trimester of pregnancy<sup>17</sup>.

In this study, it was evident that hepatitis E virus infection resulted in multiple maternal and fetus outcomes. As, result depicted that many maternal outcomes i.e PPH, DIC and hepatic encephalopathies were evident. Hepatitis E virus caused many adverse consequences threatening mother's life. Present study clearly revealed that PPH was major threat attributable to hepatitis E infection, as 30% women suffered with PPH. A study conducted on hepatitis E virus infection related to maternal outcomes show consistent results and found PPH a priority cause of hepatitis E infection during pregnancy<sup>18</sup>.

Findings of this study show that hepatitis E virus infection lead to terminate the pregnancy and preterm SVD were followed in majority cases i.e 63.33%. Induction of labour was done in 7 cases out of 60 so, it was second common mode to termination. These results are similar with other studies showing preterm SVD as common mode of pregnancy termination due to hepatitis E virus infection<sup>19</sup>.

Fetal morbidities ascribed to hepatitis E infection were also shown in this study. Rate of normal healthy births was found as 56.67% in babies with mothers affected of Hepatitis E virus. Also, results depicted cases of IUD in this study. 8 cases of IUD and 10 of neonatal deaths were revealed in present study out of total 60 cases. ERCP done in 2 while 6 cases dealt with conservative management. Another study by Farshadpour et al. proved the fatal outcomes of hepatitis E infection on fetus morbidity & mortality. Hepatitis E results in devastating effects endangering the fetus life<sup>20</sup>.

## CONCLUSION

Hepatitis E virus infection result in overwhelming effects during pregnancy threatening the life of both mother and fetus. High mortality rate was evident in hepatitis E virus infection affected pregnancies in this study. Best measures is to save life following the safety precautions and avoiding transmission of infection. There is a need to educate pregnant ladies regarding preventive measures to avoid fulminant consequences. Emphasis should be given to follow hygienic practices during pregnancy and proper antenatal visits are mandatory to educate the women.

### Authors Contribution:

II & GH conceived, designed and did statistical analysis

SS & SS did data collection & manuscript writing

SS did review and final editing of manuscript

### Grant Support & Financial Disclosures: None

## REFERENCES

- Berglöv A, Hallager S, Weis N. Hepatitis E during pregnancy: maternal and foetal case-fatality rates and adverse outcomes—a systematic review. *Journal of viral hepatitis*. 2019 Nov;26(11):1240-8.
- Bigna JJ, Modiyinji AF, Nansseu JR, Amougou MA, Nola M, Kenmoe S, Temfack E, Njouom R. Burden of hepatitis E virus infection in pregnancy and maternofetal outcomes: a systematic review and meta-analysis. *BMC pregnancy and childbirth*. 2020 Dec;20(1):1-1.
- Yasmeen T, Hashmi HA, Taj A. Fetomaternal outcome with hepatitis e in pregnancy. *J Coll Physicians Surg Pak*. 2013 Oct 1;23(10):711-4.
- Kumar A, Devi SG, Kar P, Agarwal S, Husain SA, Gupta RK, Sharma S. Association of cytokines in hepatitis E with pregnancy outcome. *Cytokine*. 2014 Jan 1;65(1):95-104.
- Shinde NR, Patil TB, Deshpande AS, Gulhane RV, Patil MB, Bansod YV. Clinical profile, maternal and fetal outcomes of acute hepatitis e in pregnancy. *Annals of medical and health sciences research*. 2014;4(8):133-9.

6. Bose PD, Das BC, Kumar A, Gondal R, Kumar D, Kar P. High viral load and deregulation of the progesterone receptor signaling pathway: association with hepatitis E-related poor pregnancy outcome. *Journal of hepatology*. 2011 Jun 1;54(6):1107-13.
7. Kar P, Sengupta A. A guide to the management of hepatitis E infection during pregnancy. *Expert Review of Gastroenterology & Hepatology*. 2019 Mar 4;13(3):205-11.
8. Sayed IM, El-Mokhtar MA, Mahmoud MA, Elkhawaga AA, Gaber S, Seddek NH, Abdel-Wahid L, Ashmawy AM, Alkareemy EA. Clinical outcomes and prevalence of Hepatitis E Virus (HEV) among non-AC hepatitis patients in egypt. *Infection and Drug Resistance*. 2021;14:59.
9. Aslan AT, Balaban HY. Hepatitis E virus: Epidemiology, diagnosis, clinical manifestations, and treatment. *World Journal of Gastroenterology*. 2020 Oct 7;26(37):5543.
10. Webb GW, Kelly S, Dalton HR. Hepatitis A and Hepatitis E: Clinical and epidemiological features, diagnosis, treatment, and prevention. *Clinical Microbiology Newsletter*. 2020 Nov 1;42(21):171-9.
11. Obiri-Yeboah D, Asante Awuku Y, Adu J, Pappoe F, Obboh E, Nsiah P, Amoako-Sakyi D, Simpore J. Sero-prevalence and risk factors for hepatitis E virus infection among pregnant women in the Cape Coast Metropolis, Ghana. *PLoS one*. 2018 Jan 25;13(1):e0191685.
12. Lhomme S, Marion O, Abravanel F, Izopet J, Kamar N. Clinical manifestations, pathogenesis and treatment of hepatitis E virus infections. *Journal of clinical medicine*. 2020 Feb;9(2):331.
13. Karna R, Hazam RK, Borkakoti J, Kumar A, Kar P. A 5-year single-center experience of hepatitis E virus infection during pregnancy. *Journal of Clinical and Experimental Hepatology*. 2020 Mar 1;10(2):135-8.
14. Goel A, Aggarwal R. Hepatitis E: epidemiology, clinical course, prevention, and treatment. *Gastroenterology Clinics*. 2020 Jun 1;49(2):315-30.
15. Cheung CK, Wong SH, Law AW, Law MF. Transfusion-transmitted hepatitis E: What we know so far?. *World Journal of Gastroenterology*. 2022 Jan 7;28(1):47.
16. Ahmad T, Hui J, Musa TH, Behzadifar M, Baig M. Seroprevalence of hepatitis E virus infection in pregnant women: a systematic review and meta-analysis. *Annals of Saudi medicine*. 2020 Mar;40(2):136-46.
17. Zaman K, Dudman S, Stene-Johansen K, Qadri F, Yunus M, Sandbu S, Gurley ES, Overbo J, Julin CH, Dembinski JL, Nahar Q. HEV study protocol: design of a cluster-randomised, blinded trial to assess the safety, immunogenicity and effectiveness of the hepatitis E vaccine HEV 239 (Hecolin) in women of childbearing age in rural Bangladesh. *BMJ open*. 2020 Jan 1;10(1):e033702.
18. Aggarwal R, Goel A. Natural history, clinical manifestations, and pathogenesis of hepatitis E virus genotype 1 and 2 infections. *Cold Spring Harbor perspectives in medicine*. 2019 Jul 1;9(7):a032136.
19. Khan SA, Khan Z, Alam Z, Sana H, Ali M, Zaman N, Ualivveya D, Rizwan M, Suleman M. Hepatitis E virus sero-prevalence among pregnant women in Khyber Pakhtunkhwa Pakistan. *Clinical Immunology Communications*. 2022 Apr 4.
20. Farshadpour F, Taherkhani R, Ravanbod MR, Eghbali SS, Taherkhani S, Mahdavi E. Prevalence, risk factors and molecular evaluation of hepatitis E virus infection among pregnant women resident in the northern shores of Persian Gulf, Iran. *PLoS One*. 2018 Jan 12;13(1):e0191090.