

ORIGINAL ARTICLE

Characteristics and Obstetric Outcomes in Pregnant Women with Acute Hepatitis E Virus Infection in Tertiary Care Hospital of Himachal Pradesh

Rajesh Kashyap^{1*}, Ivan Joshi², Dalip Gupta³, Anupam Prashar⁴, Santosh Minhas⁵

Abstract

Background: Hepatitis E Virus (HEV) infection is a major concern regarding morbidity and mortality among pregnant women especially in developing countries. The objective of this study was to determine the characteristics and obstetric outcomes in pregnant women with Acute Hepatitis E Virus Infection in tertiary care hospital of Himachal Pradesh.

Methods: Prospective observational study has been done in the department of Obstetrics and Gynaecology and department of Medicine and Emergency Medicine among all the pregnant women who were sero-positive for hepatitis E viral marker in two consecutive years. Information regarding basic characteristics of pregnant women and obstetric outcome has been collected.

Results: Among 30 pregnant women with hepatitis E viral infection, a case fatality ratio of 8.0% for hepatitis E infection was found. 13.3% of the pregnancies ended up as intra uterine death. Most common age group affected was below 25 years. Mode of delivery among 70% of the women was normal vaginal delivery though 30% women delivered prematurely.

Conclusions: This prospective case series of 30 pregnant women with acute hepatitis E viral infection, indicate poor maternal, obstetric and foetal outcome among pregnant women with hepatitis E viral infection.

Background

Hepatitis E virus (HEV) is a hepatotropic single-stranded RNA virus causing acute viral hepatitis worldwide.¹ Disease occur either in the form of large-scale epidemics related to contamination of water supplies or in the form of sporadic cases in the absence of discernible outbreaks.² Each year more than 20 million estimated cases of HEV infection occur globally, resulting into more than 55, 000 deaths.^{3,4}

In men and non-pregnant women, the disease is usually self-limited and has a low case-fatality rate (0.1%).⁵ However in pregnant women especially in the third trimester, HEV infection is more severe, often leading to fulminant hepatic failure and maternal death in up to 15% to 20% of cases.⁶⁻⁸ Although the mechanism of liver injury is not yet clear, it is possible that interplay of hormonal and immunologic changes during pregnancy, along with a high

viral load of HEV, renders the woman more vulnerable.^{7,9} This high mortality rate was first reported in an epidemic setting in the early 1980s and was reported again in a sporadic setting in 2003.^{10,11}

Information is limited and conflicting on the effect of HEV infection on maternal, obstetric, and foetal outcomes.^{12,13} Therefore, in this study we describe characteristics of HEV infected pregnant women presented to department of Obstetrics and Gynaecology, Medicine and Emergency Medicine of a tertiary care hospital of Himachal Pradesh. Obstetric, maternal and foetal outcomes among these women with acute viral hepatitis have also been determined.

Methods

This prospective observational study has been done in the department of Obstetrics and Gynaecology, Medicine and Emergency Medicine at Indira Gandhi Medical College Shimla, Himachal Pradesh, India.

All the pregnant women who were sero-positive for hepatitis E viral marker in last two consecutive years have been included in the study i.e. April 2014 through March 2016. Information regarding basic characteristics of pregnant women (like age, parity, gestational period), obstetric, maternal and foetal outcome has been collected from patient's information sheet of department.

These women were managed according to the management protocol of the Institution. Information gathered had only been used for the purpose of this study after taking permission from hospital administrations. The data collected was analysed with the help of MS Excel software. The analyses were done for calculating frequencies and percentages.

Observation

Total 30 pregnant women with hepatitis E viral infection has been observed during study period. Majority (63.3%) of the case were in year 2016. Mean age of study population was 25.34 (SD=3.94) years ranging from 19 years and to 34 years.

Most (46.7%) of pregnant women with hepatitis E viral infection were less than 25 years of age. Only 13.3% (n=04) were of the age 30 and above. 57.7% (n=17) of them were having

¹Professor, ²Junior Resident, ³Professor, Department of Medicine, ⁴Professor, Department of Community Medicine, ⁵Professor and Head, Department of Obstetrics and Gynaecology, Indira Gandhi Medical College, Shimla, Himachal Pradesh; *Corresponding Author
Received: 15.12.2016; Accepted: 17.08.2017

Table 1: Characteristics of pregnant women with Hepatitis E viral infection

	Frequency	%age
Age Groups		
<25 years	14	46.7
26-30 years	12	40.0
>30 years	04	13.3
Gravida		
Primigravida	17	57.7
Multigravida	13	43.3
Period of infection		
First trimester	01	3.3
Second trimester	08	26.7
Third trimester	07	23.3
Postpartum	14	46.7

their first pregnancy i.e. primigravida. 53.7% (n-16) of the participants were diagnosed during ante partum period of pregnancy while 46.6% (n-14) were diagnosed during postpartum period. During ante partum 26.7% (n-08) and 23.3% (n-07) cases were diagnosed during second and third trimester respectively (Table 1).

Most of the women delivered normally (70%) followed by Lower segment caesarean section in 6.7%. Among all 46.7% (n-14) of the women delivered full term while 30% (n-09) delivered prematurely. Regarding maternal outcome 76.7% (n-23) women recovered from disease without significant morbidity while 13.3% (n-4) were referred to higher centre pertaining to their progressive health deterioration. 6.67% (n-2) women died during the course of illness causing a case fatality ratio of 8.0% for hepatitis E infection (excluding all the referred/DOR cases from denominator). Both the deaths occurred in postpartum period. 43.3% (n-13) new born delivered were healthy while 20% (n-6) newborn needed hospitalization. There were 4(13.3%) intra uterine deaths. Information regarding referred or missed cases had not been found for analysis (Table 2).

Discussions

Majority of the cases of HEV has been reported in the year 2016, period that coincides with the outbreak of Hepatitis E virus infection in Shimla city leading to massive morbidity and mortality.^{14,15} In our study 46.7% of patients were below 25 years of age and were primigravida (57.7%). In regions with high disease endemicity like India, symptomatic infection is most common in young adults (aged 15–40

Table 2: Obstetrics, maternal and foetal outcome among study participants

	Frequency	%age
Mode of delivery		
NVD	21	70
LSCS	02	6.7
Other	07	23.3
Time of delivery		
Full term	14	46.7
Preterm	09	30
Other	07	23.3
Maternal out come		
Recovered	23	76.7
Referred	04	13.3
Death	02	6.7
Other	01	3.3
Foetal outcome		
Normal	13	43.3
IUD	04	13.3
Alive but need hospitalization	06	20
Other	07	23.3

years) and pregnant women.¹⁶ Mishra et al also reported majority (60%) of the hepatitis E infection among Indian pregnant women in below 25 years of age and which is in consistent with findings of our study. Severity of HEV infection among primigravida and third trimester of pregnancy has been reported higher by Mishra et al.¹⁷

In current study infection had been diagnosed both in ante partum (53.3%) and postpartum (46.7%) period of pregnancy (mostly second and third trimester of pregnancy). Hepatitis E virus has been known to infect women throughout pregnancy but case fatality rates as high as 20–25% has been reported in their third trimester.¹⁶

Most common mode of delivery was normal vaginal delivery which is common finding in most of the studies in similar settings. 30% of the women delivered prematurely in this study. Mishra et al and Jaiswal et al also reported approximately one third of the pregnant women with hepatitis E viral infection to deliver prematurely.^{17,18} However Patra et al in their study had reported preterm delivery among 90% of the cases in similar condition.⁶

Case fatality of 8.0% has been determined in current study. Poor foetal outcome has been found among 13.3% (intra uterine death) of the traced cases. Also 20% of the newborn needed hospitalization (most common reason being low birth weight and prematurity) in current study. These numbers could have varied as 13.3% of the serious women were referred to higher institute

while one left against medical advice. Maternal death among different studies in India has been reported upto 15% to 20% of women with hepatitis E viral infection.⁶⁻⁸ Patra et al. in New Delhi reported 15-20% maternal mortality rate in pregnant patients with HEV. Banait et al in Mumbai reported 69% perinatal mortality and 54% maternal mortality in HEV in pregnancy which is much higher than our results.¹⁹ Beniwal et al reported mortality rate in the range of 30.0-45.0% and may be as high as 70.0%.²⁰ Ahmed et al reported 25% maternal mortality rate and 17.8% intrauterine deaths in pregnant HEV positive mothers.²¹ Shukla et al reported 33.3% maternal mortality rate in patients with hepatitis E in pregnancy.²² Foetal outcome in our study has been found relatively better than reported from other studies. Patra et al reported stillbirth in 54% of cases while Mishra et al reported perinatal mortality of 24%.^{18,6}

Various immunologic and hormonal changes during pregnancy impair cellular immunity by triggering adapter protein (ORF3 of HEV), which could facilitate viral replication and lead to release of cytokines and liver cell apoptosis causing significantly higher morbidity and mortality.²³⁻²⁵

Hepatitis E infection during the pregnancy is a life threatening condition. This prospective series of 30 pregnant women with acute hepatitis E viral infection, indicate poor maternal, obstetric and foetal outcome among pregnant women with hepatitis E viral infection. There is urgent need of promoting awareness regarding this preventable disease. Sufficient medical facilities for its early detection as well as for aggressive prompt treatment have to be established at least at secondary and tertiary health care institutes. The early diagnosis and improvement in case management are keys to reduce morbidity and mortality of hepatitis E infection in pregnancy.

References

1. Khuroo MS. Study of an epidemic of non-A, non-B hepatitis. Possibility of another human hepatitis virus distinct from post-transfusion non-A, non-B type. *Am J Med* 1980; 68:818-24.
2. Agrawal R. Hepatitis E in pregnancy. *Indian Journal of Gastroenterology* 2007; 26:3-5.
3. Rein DB, Stevens GA, Theaker J, Wittenborn JS, Wiersma ST. The Global Burden of Hepatitis E Virus Genotypes 1 and 2 in 2005. *Hepatology* 2012; 55:988-97.
4. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans

- V, Abraham J, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012; 380:2095-2128.
5. Krawczynski K, Aggarwal R, Kamili S. Hepatitis E. *Infect Dis Clin North Am* 2000; 14:669-87.
 6. Patra S, Kumar A, Trivedi SS, Puri M, Sarin SK. Maternal and fetal outcomes in pregnant women with acute hepatitis E virus infection. *Ann Intern Med* 2007; 147:28-33.
 7. Devi SG, Kumar A, Kar P, Husain SA, Sharma S. Association of pregnancy outcome with cytokine gene polymorphisms in HEV infection during pregnancy. *J Med Virol* 2014; 86:1366-76.
 8. Teo CG. Fatal outbreaks of jaundice in pregnancy and the epidemic history of hepatitis E. *Epidemiol Infect* 2012; 140:767-87.
 9. Fiore S, Savasi V. Treatment of viral hepatitis in pregnancy. *Expert Opin Pharmacother* 2009; 10:2801-9.
 10. Khuroo MS, Teli MR, Skidmore S, Sofi MA, Khuroo MI. Incidence and severity of viral hepatitis in pregnancy. *Am J Med* 1981; 70:252-5. [PMID: 6781338].
 11. Khuroo MS, Kamili S. Aetiology, clinical course and outcome of sporadic acute viral hepatitis in pregnancy. *J Viral Hepat* 2003; 10:61-9.
 12. Acharya SK, Dasarathy S, Kumer TL, Sushma S, Prasanna KS, Tandon A, et al. Fulminant hepatitis in a tropical population: clinical course, cause, and early predictors of outcome. *Hepatology* 1996; 23:1448-55.
 13. Khuroo MS, Kamili S. Aetiology and prognostic factors in acute liver failure in India. *J Viral Hepat* 2003; 10:224-31.
 14. Bisht G. Shimla battles worst jaundice outbreak since 1947. *Hindustan Times*. February 2016. Available with <http://www.hindustantimes.com/india/shimla-battles-worst-jaundice-outbreak-since-1947/story-l3LhFdiCO0TjuYGaYXs8sK.html> Accessed on 25.11.2016.
 15. Sharma A. Jaundice outbreak in Shimla: 10 dead. *The Indian Express*. February 2016. Available with <http://indianexpress.com/article/india/india-news-india/jaundice-outbreak-in-shimla-10-dead/> Accessed on 25.11.2016.
 16. World health organization. Hepatitis E fact sheet. Available with <http://www.who.int/mediacentre/factsheets/fs280/en/> Accessed on 15.11.2016.
 17. Mishra S, Jha RK, Thakur R, Tiwari S. Study of maternal and prenatal outcome in pregnant women with acute hepatitis E viral infection. *Int J Reprod Contracept Obstet Gynecol* 2016; 5:2300-3.
 18. Jaiswal SP, Jain AK, Naik G, Soni N, Chitnis DS. Viral hepatitis during pregnancy. *Int J Gynecol Obstet*. 2001;72:103-8.
 19. Banait VS, Sandur V, Parikh F, Ranka P, Sasaidharan, Sattar A, et al. Outcome of acute liver failure due to acute hepatitis E in pregnant women. *Indian J Gastroenterol* 2007; 26:6-10.
 20. Beniwal M, Kumar A, Kar P, Jilani N, Sharma JB. Prevalence and severity of acute viral hepatitis and fulminant hepatitis during pregnancy: a prospective study from North India. *Indian J Med Microbiol* 2003; 21:184-5.
 21. Ahmed RE, Karsny MS, Adam I. Brief report: acute viral hepatitis and poor maternal and perinatal outcome in pregnant Sudanese women. *J Med Virol* 2008; 80:1747-8.
 22. Shukla S, Mehta G, Jais M, Singh A. Prospective study on acute viral hepatitis in pregnancy: seroprevalence and fetomaternal outcome of 100 cases. *J Biosci Tech* 2011; 2:279-86.
 23. Pal R, Aggarwal R, Naik SR, Das V, Das S, Naik S. Immunological alterations in pregnant women with acute hepatitis E. *J Gastroenterol Hepatol* 2005; 20:1094-101.
 24. Gelpi AP. Viral hepatitis complicating pregnancy: mortality trends in Saudi Arabia. *Int J Gynaecol Obstet* 1978; 17:73-7.
 25. Nayak NC, Panda SK, Datta R, Zuckerman AJ, Guha DK, Madanagopalan N, et al. Aetiology and outcome of acute viral hepatitis in pregnancy. *J Gastroenterol Hepatol* 1989; 4:345-52.