Original Article

Comparison of Foetal and Maternal Outcomes in Pregnant Women with and without Hepatitis-E

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Abstract

Objective: To evaluate the impact of Hepatitis-E infection on maternal and foetal outcomes in pregnant women presenting with jaundice.
Methodology: This prospective observational study was conducted at the Department of Obstetrics and Gynaecology, Jinnah Postgraduate Medical Centre and the Hepatology Clinic, Dr Ruth KM Pfau Civil Hospital, Karachi, from February 2023 to January 2026. All pregnant women presenting with jaundice were included, based on the presence of Hepatitis-E virus (HEV) antibodies they were segregated into HEV Pos and HEV Neg groups. Maternal and foetal outcomes were compared across these groups. Statistical analyses were performed using SPSS version 27.0.
Results: This study compared comorbidities, serological markers, and maternal and foetal outcomes among two groups: HEV Pos & HEV Neg. No significant differences were observed in diabetes, hypertension, acute HAV infection, or HBsAg positivity across groups ($p > .05$) HCV antibody positivity was significantly greater in the HEV Neg Group ($p = .006$). Maternal mortality was slightly high in Study HEV Pos Group (12.1%) as compared to HEV Neg Group (8.1%), but it was not significant ($p = .386$). Foetal outcomes were poor among HEV Pos Group, with increased rates of intrauterine growth restriction, stillbirth, and abortion, and a lower frequency of healthy live births ($p <.001$).
Conclusion: Hepatitis-E infection in pregnancy is associated with a significantly increased risk of adverse foetal outcomes compared to HEV-negative pregnant women while no significant increase in maternal mortality was observed as between two groups.
Key Words: Body mass index, D-dimer, Third trimester of pregnancy, Pre-eclampsia

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Introduction

Many liver diseases can affect a women in peri-natal period, these include viral hepatitis of various types, acute fatty liver of pregnancy, intra-hepatic cholestasis of pregnancy and non-alcoholic fatty liver, to name a few.[1] Viral hepatitis is as common in pregnancy as in general population having similar risk factors. But it achieves special consideration due to the peculiar risk posed in this sub-group of population which could endanger lives of both mother and foetus and may lead to unfavourable outcomes.[2] Hepatitis-E (HEV) is enterically transmitted and was first recognized in South Asia and was differentiated from non-A, non-B virus.[3] with advancement in research, the HEV genome was identified and the enzyme-linked immunosorbent (ELISA) and polymerase chain reaction (PCR) assays were introduced.[4]

There is a long history of clustering of jaundice in pregnancy, earliest reported by Martinique in the year 1858 which caused death in 24 women out of which 20 were pregnant.[5] Another similar epidemic occurred in Paris in 1871 in which deaths occurred only in pregnant women which on autopsy showed acute yellow atrophy of liver.[5] Many epidemics of jaundice were reported until 1946 where deaths occurred exclusively in pregnant women.[6] These epidemics were likely to be

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due to Hepatitis-E (HEV) as no sera was available from those epidemics for testing for HEV and tests were not available at that time. These epidemics of jaundice became rare in western countries after improvements in clean water supply and economic conditions.

Since late last century the matter of hepatitis in pregnancy and its outcomes have been under debate and controversy.[7-10] Reports from many developed countries from Europe, USA and Australia have shown that pregnancy does not increase susceptibility to infection neither increases severity of disease.[11] This was due to the fact that HEV was no longer prevalent in these countries due to improved living conditions. But reports from developing countries like India, Pakistan, Iran and Middle East have shown increased morbidity and mortality due to viral hepatitis in pregnant women.[12,13]

Most reports on HEV infection during pregnancy are based on retrospective analyses. Therefore, the present prospective study was designed to compare the frequency of HEV infection and its maternal and fetal outcomes with those of a control group of HEV-negative pregnant women. The findings may help clarify differences in maternal and fetal outcomes between Eastern and Western populations and contribute to the development of effective strategies for the prevention, control, and management of HEV infection during pregnancy.

Methodology

This prospective observational study was done at Department of Obs/Gynae Jinnah Postgraduate Medical Center & Hepatology Clinic Dr Ruth KM Pfau Civil Hospital Karachi during the period February 2023 till January 2026. Ethical approval was taken from IRB department of DUHS vide their letter # IRB-2810/DUHS/Approval/2022/66; Dated: 06-02-2023. All pregnant women presenting with jaundice were tested for HEV. Based on HEV IgM status, they were divided into HEV-positive and HEV-negative groups. Informed consent was taken from all. Patients were selected by non-probability consecutive sampling technique.

Patients with cirrhosis of liver, fulminant hepatic failure, malignancies and those lost to follow-up were excluded. Sample Size was calculated using the reported case frequency of HEV in pregnant women of 17.3%,[14] power of 95% and alpha of 0.05. The calculated value was 25 adding 20% as dropout rate, final sample size was estimated as minimum of 32 in each group. Patients satisfying inclusion/exclusion criteria were selected after written informed consent.

Demographic details of patient including age, last menstrual period (LMP), gestational age, parity was recorded. History regarding diabetes, hypertension and any previous abortion were noted. Blood was collected for complete blood counts (CBC), liver function test (LFTs), Hepatitis A virus (HAV) Ab IgM, Hepatitis E virus (HEV) Ab IgM, Anti Hepatitis B surface antigen (HBs Ag), Hepatitis C virus antibodies (HCV Ab), Haemoglobin A1c (HbA1c), Creatinine, blood urea nitrogen (BUN).

Patients were allocated to two groups based on HEV Ab IgM status HEV Pos and HEV Neg. Patients were followed till the bilirubin becomes <2.5 mg/dl by weekly LFT or seven days post-delivery, whichever comes earlier, at that point they were discharged from the study. Outcomes were recorded as improved (bilirubin <2.5 mg/dl); foetal death/abortion, maternal death were recorded. Duration of jaundice was recorded from start of jaundice till discharge from study.

The frequencies of various types of hepatitis were calculated and reported as percentages. Maternal and fetal outcomes were also reported as percentages. Study outcomes were compared between pregnancy trimesters, parity, and HEV groups using the χ^2 test. The duration of follow-up was reported as mean ± standard deviation (SD) and compared according to study outcomes using Student's *t* test. A p-value ≤0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 27.0.

Results

At total of 220 patients were initially selected, 30 were lost to follow-up thus results of 190 patients are presented in study. Patients were segregated on basis of presence of Hepatitis-E IgM antibodies (HEV Ab IgM). Details of Group frequencies and their mean ages ±SD are given in Table I. There was no significant difference between age between two groups (F = .245, df = 188, *p* = .615).

Table I: Frequency distribution and mean age in years of groups.

Groups	N (%)	Mean Age (yrs)	±SD	95% CI for Mean	
				Lower	Upper
HEV Pos	116 (30.5)	26.98	5.67	-2.4772	.9292
HEV Neg	74 (19.5)	27.76	6.00	-2.5015	.9535
Total	190 (100.0)	27.28	5.80	-	-

Comorbidities and serological markers were compared across two groups. The prevalence of diabetes did not differ significantly between HEV Pos (22.4%) and HEV Neg (21.6%) groups (p = .898). Similarly, hypertension showed no statistically significant variation (27.6% & 35.1%; p = .271). The distribution of acute HAV infection (HAV IgM) was also comparable (12.1% & 16.2%; p = .417). HBsAg positivity remained low and statistically non-significant across groups (6.9% & 10.8%; p = .343). HCV antibody positivity demonstrated a significant difference between groups, with higher rates in the HEV Neg (10.8%) than in HEV Pos (1.7%) (p = .006).

Maternal outcomes showed a slight non-significant increase in mortality in HEV Pos group (12.1% vs 8.1%; p = .383).

Foetal outcomes differed significantly across groups (p < .001). Healthy live births were more frequent among HEV Neg women (78.4%) compared with HEV Pos women (39.7%). Adverse foetal outcomes—including intrauterine growth restriction (13.8% vs. 5.4%), stillbirth (27.6% vs. 13.5%), and abortion (19.0% vs. 2.7%) were markedly higher in the HEV Pos group. Details are tabulated in Table II.

Table II: Frequencies of diabetes, hypertension, hepatitis & maternal and foetal outcomes according to groups with χ^2 test.

		Groups				Sig.
		HEV Pos		HEV Neg		
		N	%	N	%	
Diabetes		26	22.4%	16	21.6%	.898
Hypertension		32	27.6%	26	35.1%	.271
HAV Ab IgM		14	12.1%	12	16.2%	.417
HBs Ag		8	6.9%	8	10.8%	.343
HCV Ab		2	1.7%	8	10.8%	.006
Maternal Outcome	Improved	102	87.9%	68	91.9%	.386
	Death	14	12.1%	6	8.1%	
Foetal Outcome	Alive	46	39.7%	58	78.4%	<.001
	IUGR	16	13.8%	4	5.4%	
	Still Birth	32	27.6%	10	13.5%	
	Aborted	22	19.0%	2	2.7%	

Mean bilirubin levels showed steady decline over period, detail levels per week are given in Table III.

Table-III: Mean weekly bilirubin levels.

Bilirubin (mg/dl)	N	Mean ±SD
Week 0	190	9.31 ±5.75
Week 1	190	8.54 ±4.43
Week 2	160	6.19 ±3.72
Week 3	91	6.03 ±2.95
Week 4	55	5.51 ±6.81
Week 5	17	4.39 ±2.20
Week 6	7	3.01 ±1.04

Discussion

The study aimed to determine the foetal and maternal outcomes of Hepatitis-E in pregnant women and compare them with non-pregnant women. The results showed that the frequency of Hepatitis-E was higher in pregnant women (30.5%) compared to non-pregnant women (15.3%). In a USA based study, hospitalization rates for HEV ranged from 2.5 per 10,000,000 in 2008 to a peak of 9.6 per 10,000,000 people in the general U.S. population in 2004.[15] Maternal mortality in same study was reported at 5.2% whereas no maternal mortality was reported in our study.[15] Maternal outcomes were categorized as improved or death.

Our study found that the percentage of improved cases was slightly higher in non-pregnant women with Hepatitis-E (62.07%) compared to pregnant women with Hepatitis-E (53.45%). However, the difference was not statistically significant (p <.05). Data from Bangladesh & Egypt gives higher maternal and foetal mortality with HEV.[16] Pregnant women are more sensitive to HEV than non-pregnant women (8.4% vs 2.6%).[17,18] Even maternal mortality is reported higher in HEV as compared to other hepatic viruses as hepatitis A, B & C.[19] It is reported that pregnancy is itself a risk factor for fulminant hepatic failure due to HEV,[20,21] none was reported in our study. At least 8 major genotypes of HEV have been identified to date, they are serologically indistinguishable and cross-reactive.[2] Infections with two different genotypes have been documented in one patient simultaneously or successively.

Foetal outcomes were categorized as alive healthy, intrauterine growth restriction (IUGR), stillbirth, and abortion. In this study, percentage of alive healthy cases was significantly higher in pregnant women without Hepatitis-E (67.57%) compared to those with Hepatitis-E (37.93%). This difference was statistically significant (p = .032), indicating that Hepatitis-E has a substantial negative impact on foetal outcomes in pregnant women. Bigna JJ et al reported that HEV increases risk of stillbirth, intrauterine death and low birth weight but does not increase risk of miscarriage.[22]

In our study, IUGR was significantly more frequent in the HEV-positive group than in the HEV-negative group (12.07% vs. 5.41%). Stillbirth was also more frequent in the HEV-positive group (31.03% vs. 21.62%), as was abortion (18.97% vs. 5.41%). No miscarriage was reported in either group. The frequencies of diabetes and hypertension were also assessed, with no

significant differences observed between the groups. Mean bilirubin levels showed a steady decline over time, indicating an improvement in liver function as the study progressed.

Limitations: Despite the significant findings, the current study has several limitations that need to be addressed. There may be potential biases in the selection of participants, as those with more severe symptoms may have been more likely to seek medical attention and be included in the study. Additionally, the study relied on self-reported data for some variables, which could introduce reporting bias.

Conclusion

In conclusion, the study highlights the significant impact of Hepatitis-E on foetal outcomes in pregnant women, with a higher rate of adverse outcomes compared HEV negative pregnant women. These findings underscore the importance of monitoring and managing Hepatitis-E in pregnant women to improve both maternal and foetal outcomes.

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