Analysis of Maternal Morbidity and Mortality in Hepatitis E Virus Infection in Pregnant Women

Shikha Jain[1], Shammi Kumar Jain[2], Preeti Nigotia[3], Gorav Jain[4]

[1]Assistant Professor, Department of Obstetrics and Gynaecology, SRVS Medical College and Hospital, Shivpuri, M.P.

[2]Assistant Professor, Department of Paediatrics, SRVS Medical College and Hospital, Shivpuri, M.P.

[3]Assistant Professor, Department of Medicine, SRVS Medical College and Hospital, Shivpuri, M.P.

[4]Senior Resident, Department of Ophthalmology, SRVS Medical College and Hospital, Shivpuri, M.P.

Abstract

Aim: To analyses of maternal morbidity and mortality in hepatitis E virus infection in pregnant women.

Method: A prospective study was conducted over a period of 1 year in a tertiary care hospital of Delhi. Total of 48 HEV positive patients confirmed by anti IgM test were included .Demographic profile along with antenatal and postnatal complications of patients were studied.

Result: The mean age of women was 23.5year.The mean gestational age of women was 32 week. Mean gravidity was of the total 48 pregnant women; 38 delivered and 10 undelivered. Of these 35 was vaginal delivery (72.9%) (27 preterm, 08term) and 03 (6.25%) underwent caesarean section. Maternal morbidity were studied in terms of admission in intensive care unit 15 (31.25%) coagulopathy 04 (8.3%), postpartum haemorrhage 04 (8.3%), intrauterine growth retardation 03(6.25%), and sepsis 01(2.08%). Maternal mortality was occurred in 12 out of 48 cases (25%).While all 12 mortality reported in postnatal period, no mortality found in antenatal period. Most of postnatal death occurred due to hepatic encephalopathy (n=8) after 1 week of delivery. All these patients had hepatic encephalopathy at the time of admission. 34 babies were born alive, among them 20 (41.6%) were shifted to newborn intensive care unit (NICU).

Conclusion: Maternal prognosis is poor in HEV positive patient particularly in postnatal period. HEV infection can be prevented by good sanitation measures while development of encephalopathy can be prevented by earlier and careful evaluation of mental status .By doing this we can reduce the burden of maternal mortality to some extent.

Introduction

Hepatitis E is the commonest cause of acute clinical hepatitis in adults in India .Although infection with hepatitis A is more widespread it is often asymptomatic.

Acute liver failure (ALF) has also been called fulminant hepatic failure or acute hepatic failure, with the basic definition of the onset of hepatic encephalopathy (HE) within 8 weeks of the patient becoming jaundiced. It's typical symptoms are anorexia, dark urine, nausea, vomiting, abdominal pain and icterus with alteration in sensorium and coagulopathy in hepatic encephalopathy. The nutritional, immunological, and genetic factors play role in the path physiology of fulminant HEV during pregnancy in developing countries .The most common source of HEV infection is faecally contaminated drinking water. In developing countries, HEV genotypes 1 and 2 are spread by faecally contaminated drinking water.

An understanding of disease complications can help to formulate effective strategies for disease prevention, control and patient management leading to better fetomaternal outcome. In view of the above-stated facts, we planned to study the fetomaternal morbidity and mortality associated with hepatitis E virus infection not only during the antenatal period but also during postnatal period.

Methodology:

This prospective study was conducted in the Department of Obstetrics and Gyneacology of Deendayal Hospital Delhi, from July 2015 to June 2016.

Samples of 90 patients who presented with jaundice in pregnancy were collected and sent to laboratory for complete blood counts, coagulation profile, liver function tests , renal function tests and serological tests for IgM anti- HAV, HBs antigen, IgM anti-HEV, and IgM anti-HCV using commercially available ELISA kits.

Acute viral hepatitis E can usually be differentiated from other causes of jaundice by its marked elevations of aspartate transferase and alanine transferase (typically $\geq$ 400 IU/L), serum bilirubin >1.2 mg/dl, anti IgM >0.458, moderate elevation of alkaline phosphatase.

Women with jaundice due to cholestasis of pregnancy, pre-eclampsia, acute fatty liver of pregnancy, inflammation of bile ducts, gallstones, infiltrative disease of liver, hepatitis A, B or C were excluded from the study. Women with both anti IgM E and anti IgM A positive were also excluded. Data was collected after an informed consent from HEV positive patients who fulfilled the inclusion criteria. Personal, family and socioeconomic history was recorded in detail. Complete physical and obstetric examination was carried out.

The presence of PT prolongation or hepatic encephalopathy (grade II or higher) was ground for admission in intensive care unit (ICU).Hepatic encephalopathy was graded using west Haven criteria 1. All patients were admitted and managed in collaboration with physician.

Pregnancy termination by induction of labour or caesarean section was carried out only for obstetric indications. All patients were followed till discharge or death.

Result:

Out of a total of 90 patients admitted for jaundice; 48 pregnant women (mean age 23.5±2.5yrs) presenting with clinical and biochemical evidence of hepatitis and serologically proven HEV were included in this study. 15 (31.2%) patients were primigravida followed by gravida two in 12 (25%) cases and 11 (22.9%) patients were gravida 3 or more. Out of 48 HEV positive, 20 women (41.6%) were in the second trimester of pregnancy and 28 women (58.4%) were in the third trimester. Most of the women were belonging to poor socioeconomic status. Serum bilirubin of these patients varied between 1.5 – 26 mg/dl with mean of 15.34 ± 5.32 mg/dl, ALT ranged 24 – 1933 IU/L with mean value of 602 IU/L, AST ranged 18-3160 IU/L with mean 712 IU/L.

Maternal complications were studied

during antenatal and postnatal period in table 2 and table 3 respectively Out of 48 HEV patients 35(72.9%) were delivered vaginally (27 preterm, 08term) and 03 (6.2%) underwent caesarean section (two for failed induction and one for primi breech in labor).Induction were done for IUD, severe oligo, BPS 4/8. 10(20.8%) patients were undelivered and discharged after showing decreasing trends in liver function tests (LFTS)and was advised to follow up in OPD with weekly LFT done. Out of those 10; 05 were readmitted as preterm labor with deranged LFT but not reincluded in study, 02 continued their pregnancy up to term without any complication and 03 were lost to follow up. Morbidity reported during antenatal period were 03(6.25%) ICU admission, 03(6.25%) IUGR, 04(8.3%) IUD, 02 (4%) coagulation failures, 01(2.08%) chorioamnionitis. No mortality was reported in antenatal patients. However in all 03 ICU patients and patient with chorioamnionitis mortality occurred later on in postnatal period.

IN table 3 postnatal complications were studied. Out of total 38 delivered patients; 12 (25%) mortality occurred. Most were because of hepatic encephalopathy(HE) leading to coma due to fulminant liver failure after one week of delivery.02 (4.1%) maternal deaths were occurred due to disseminated intravascular coagulation (DIC) because of coagulation failure.01 maternal death was because of pulmonary embolism due to venous thrombosis of leg on 18th day of delivery confirmed by Doppler of legs.01 death was because of multiorgan failure due to sepsis on 6th postnatal day.04 patients out of 38(10.5%) had PPH during intrapartum and postpartum period managed conservatively.22 patients had uneventful period after delivery and were discharged.

Foetal outcome in patients infected with acute hepatitis E in pregnancy is shown in Figure 4. Among 34 alive babies, 20(58.8%) were admitted to NICU. Out of 20 NICU admissions; 16 were admitted for low birth weight and 04 for birth asphyxia. Rest of the 11 preterm babies (Birth wt. >1.5 kg) were shifted to mother side.

Table 1: Demographic & Lab Parameters

VARIABLES	MEAN (SD)	RANGE
Age	23.5 (2.5)	19 – 36 (yrs)
Gravidity	02	1 – 5
Gestational Age	32 (5.02)	16 – 42 (wks)
II Trimster (n = 20)		
III Trimster (n = 28)		
Total Bilirubin	15(5.3)	1.5-26(mg%)
Alanine Transferase	602	24 – 1933 (IU/L)
Aspartate Transferase	712	18 – 3160 (IU/L)

Table 2: Pregnancy Outcome

Outcome	Number (n = 48)	Percentage(%)
Vaginal Delivery	35/48	72.92 %
Cesarean section	03/48	6.25 %
Undelivered Improved & Discharged	10/48	20.83 %
Antenatal Mortality	00	-

Table 3: Pregnancy Outcome of 10 Undelivered Patients on follow up

Outcome	Number (n = 10)	Percentage(%)
Preterm Delivery	05/10	50 %
Term Delivery	02/10	20 %
Lost to Follow Up	03/10	30 %

Table 4: Perinatal Outcome

Outcome	Number (n = 38)	Percentage(%)
Born alive	34/38	89.47 %
IUD	04/38	10.53 %
Term Baby	11/38	28.95 %
Preterm	27/38	71.05 %
Admission to NICU	20/38	52.63 %

Table 5: Maternal Complication

Complication	Number (n=48)	Percentage(%)
Chorioamnionitis	01/48	2.08 %
IUGR	03/48	6.25 %
PPH	04/48	8.33 %
Pulmonary Embolism	01/48	2.08 %
DIC	02/48	4.17 %
Sepsis	04/48	8.33 %
Encephalopathy	08/48	16.67 %
Death (Post Natal)	12/48	25 %

Table 6: Cause of Death

Cause of	Number (n=48)	Percentage(%)
Encephalopathy	08/48	16.67 %
DIC	02/48	4.17 %
Pulmonary Embolism	01/48	2.08 %
Sepsis	01/48	2.08 %

Discussion:

Hepatitis E is usually self-limiting but may develop into fulminant hepatitis (acute liver failure) especially in pregnancy. The hepatitis E virus is transmitted via the faecal-oral route, principally via contaminated water. Hepatitis E is found worldwide, but the prevalence is highest in East and South Asia. [1]

Our study had 90 cases of jaundice out of which 48(53.4%) were due to HEV. This is comparable with the findings of the various studies, who reported the incidence of HEV infection in pregnancy from 45% to more than 50% [2]. The reason for it may be that pregnancy is associated with high levels of steroid hormones. These steroid hormones may promote viral replication. [3]

In our study 26 patients (54.1%) had preterm deliveries between 25 – 35 weeks of gestation. Study by Oladokun et al [4] and Parveen et al [5] have reported 39.6% and 71.1% of preterm deliveries respectively. It was also observed in our study that most of the patients were illiterate, unbooked and belonged to low socioeconomic class, living in areas with poor sanitation. This accounts for a higher prevalence of HEV infection in these women. Malnutrition superimposed on

the normal demands of pregnancy and inversion of T and B lymphocytes in early pregnancy have been postulated to be the

contributing factors [6].

Our maternal mortality rate was 25 %(12 /48). Kamalajayaram and Rama Devi reported 33.3% and Singh et al reported 10% mortality rate in there studies [7,8]. In our study no death in antenatal period was found, However 03 patients with grade III/ IV encephalopathy were shifted to ICU. 02 IUD patients developed coagulation failure treated by transfusion of blood products.

Most common cause of mortality was hepatic encephalopathy due to acute liver failure seen in 08(16.67%) patients .Out of 08 patients 02 had grade III and 01 had grade IV encephalopathy at the time of admission. Patient with grade IV HE had IUD induced delivery on day 03 of ICU stay .02 patient with HE grade III had spontaneous preterm delivery on day 5th , 6th day respectively. Rest 04 patients had grade I and 01 patient had grade II HE respectively at the time of admission, admitted to ICU after delivery because of not responding to treatment .All patients developed higher grades of encephalopathy and despite best possible treatment went in to coma and finally death after 1-2 weeks of delivery. Anshuja et al [9] and sultana et al [10] also reported hepatic encephalopathy is the most common cause of death in viral hepatitis .All maternal deaths in this group of patients had initial serum bilirubin level of ≥ 15. It shows that maternal mortality is directly related to the serum bilirubin level.

Out of the 04 women with DIC who were treated by transfusion of fresh frozen plasma, 02 woman (4.12%) died despite management on 3rd, 4th day of delivery. Tripti et al [11] reported DIC 21% in his study which is consistent with our study.

01 patient (2.01%) on 16th day developed unilateral pain , swelling over left leg, homans sign was positive, d dimer test was positive. Color dopler of leg revealed deep venous thrombosis .Anticoagulants was started, leg elevation was done but patient was developed pulmonary embolism and expired after 2 days.01 patient (2.01%)died because of sepsis already set in antenatal period admitted with chorioamnionitis. All 12 mortality were seen in the postnatal period i.e. high postnatal mortality also reported in study done by Sultana et al10. This observation can partly be explained by the fact that process of multiorgan failure has been already initiated in antepartum period. However, exact underlying mechanism for this deterioration is not yet known Among the 20 NICU admission 06 died within one week along with the 4 IUD contributes to 10 perinatal deaths out of 38 deliveries of HEV positive mother. This high perinatal mortality is similar to the study reported by Tahira et al [12].

To summarize as HEV infection can by prevented by good sanitation measures ,while development of encephalopathy can be prevented by earlier and careful evaluation of mental status .By doing this we can reduce the burden of maternal mortality to some extent. Attacks are often precipitated by infection or constipation. Hepatic encephalopathy is reversible with treatment. [13]

All delivered patients should receive crucial care in collaboration with physician. .Early and timely diagnosis coupled with multidisciplinary approach to the management can save life of the mother and foetus.

References:

1. Ferenci P, Lockwood A, Mullen K, Tarter R, Weissenborn K, Blei AT. Hepatic encephalopathy—definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. HEPATOLOGY 2002;35:716-721.
2. Beniwal M, Kumar A, Kar P et al. Prevalence and severity of acute viral hepatitis and fulminant hepatitisduring

pregnancy: A prospective study from North India. Ind J Med Microbiol 2003;21:184-5.

3. Khuroo MS, Kamili S, Yattoo GN. Hepatitis E virus infection may be transmitted through blood transfusions in an endemic area. J Gastrroenterol Hepatol 2004; **19**: 778-84.

4. Oladokun A, Otegbayo JA, Adeniyi AA. Maternal & fetal outcome of Jaundice in pregnancy at university college Hospital, Ibadan. Niger J Clin Pract. 2009;12(3):277-80.

5. Parveen T, Begum F, Akhtar N. Feto-maternal outcome of jaundice in pregnancy at tertiary care hospital. Mymensingh Med J. 2015;24(3):528-36.

6. Strelkauskas AJ, Darties IJ, Dray S. Longitudinal studies showing alterations in the levels and functional response of T and B lymphocytes in human pregnancy. Clin Exp Immunol 1978;32:531-39.

7. Kamalajayaram V, Rama Devi A. A study of maternal mortality in jaundice. J Obstet Gynecol India 1988;38:439-41.

8. Singh S, Chauhan R, Patel RS.

9. Singla A , Mehta S , Rajaram S. et al. Materno-Fetal Outcomes with Viral Hepatitis in Pregnancy . J Obstet Gynecol India(May–June 2016) 66(3):166 – 169.

10. Sultana R, Humayun S. Fetomaternal Outcome in Acute Hepatitis E. JCPSP 2014; 24 (2): 127-130.

11. Nagaria T, Agrwal S. Fetomaternal outcome in Jaundice during Pregnancy. J Obstet Gynecol India. 2005;55:424-7.

12. Tahira Y, Haleema A. et al .Fetomaternal Outcome with Hepatitis E in Pregnancy .Journal of the College of Physicians and Surgeons Pakistan 2013, Vol. 23 (10): 711-714.

13. Namukwambi, R. N., Tuhadeleni, O., & Van Neel, R. (2022). The Knowledge and Practices of Handwashing Among Street Food Vendors in the Keetmanshoop Municipal Area: none. Journal of Medical Research and Health Sciences, 5(4), 1860–1865. https://doi.org/10.52845/JMRHS/2022-5-4-1

Jaundice in pregnancy. J Obstet Gynecol India 1991;41:187-95.