Feto-Maternal Outcome in HEV Infection

Malahat Mansoor,[1] **Hammad Raza,**[2] **Rubina Tariq**[3]

Abstract

Objective: To observe feto-maternal outcome in HEV +ve patients.
Study Design: Observational Study.
Place and Duration of Study: Sir Ganga Ram Hospital, Lahore from May 2008 to May 2010.
Patients and Methods: This study included all pregnant in whom HEV IgM / IgG diagnosed and presented with raised bilirubin (> 2g/dl). Their course of illness and fetal outcome was measured.
Results: Out of 33 patients, 54% were less than 25 years and 31% (10/33) were upto 30 years. 15% (5/33) were above 30 years. Parity showed (36.63) ratio between primigravida and multigravida. 7/33 were less than 28 weeks gestation in whom only maternal outcome was studies and rest 26/33 were 28 and more weeks pregnant. Out of 26 patients, 5 babies were found dead in utero and 5 babies expired later on. (38% perinatal mortality). Perinatal morbidity in term of RDS, ANN and jaundice was found in 76% (16/26) babies. A total of 10/33 patients developed worsening of conditions with 6 having DIC, 2 with post partum hemorrhage and 2 with fulminant hepatic failure who expired and 6% mortality in mothers was observed and they were in last trimester.
Conclusion: HEV infection during pregnancy is a high risk condition for both mother and baby.
Key Words: HEV (Hepatitis E virus) ANN (asphysxia neonatorum) RDS (Resp Distress syndrome).

Mansoor M.[1]
Assistant Prof Gynae Unit – I, Services Medical College, Lahore

Raza H.[2]
Associate Prof. Medicine Unit – I, Sir Ganga Ram Hospital/ FJMC, Lahore

Tariq R.[3]
Assistant Prof. Medicine Gynae Unit – I, Services Medical College, Lahore

Introduction

Hepatitis E is a single stranded RNA virus and is one of the causes of jaundice in pregnancy.[1] This virus has caused large scale epidemics and sporadic cases of acute viral hepatitis in developing countries.[2] Its specific diagnosis depends on the detection of specific serological markers which are IgM HEV for acute and chronic hepatitis status respectively. Hepatitis E virus like Hepatitis A virus is spread by faeco-oral route and in non-pregnant women and men, the disease is usually self limiting and has a low case-fatality rate (< 0.1%).[3]

However, HEV has the propensity to cause severe disease in pregnancy. In some regions of the world, transmission occurs via faecal continuation during pregnancy. Sexual contact my play insignificant role in causing HEV infection.

In pregnant patients, the worsening of HEV in pregnancy has been reported mostly in under – developed countries like North Africa, India, Pakistan, Ghana and Egypt. Whether the severe outcome in pregnancy in these countries reflects virus virulence, variants or host factors especially malnutrition or failure of timely and proper treatment remains inconclusive.[4]

Vertical transmission and mother – to – child transmission may occur either due to viral transmission in utero or ingestion of infected maternal blood during delivery by the fetus. Immuno prophylaxis against HEV is not available. Hence pregnant women are best advised to avoid contact with suspected HEV cases

and it can be minimized by adapting hygienic habits like washing hands, fruits and vegetables before eating.

Disposing of contaminated clothes and fomites by autoclaving and incineration also helps to prevent HEV infection.

Overall management of HEV during pregnancy is no different from managing jaundice due to other causes of viral hepatitis. But has been generally observed that HEV in pregnancy can be aggressive.

Maternal and Methods

The study was conducted at Sir Ganga Ram Hospital for a period of two years i.e May 2008 to May 2010. Pregnant patients with acute viral hepatitis and with + ve IgM HEV antibodies were included. Patients were initially admitted for evaluation and investigations and also to treat any feto-maternal complications. These patients were investigated for blood group and Rh factor, Complete count (CBC), Blood sugar random, urine complete examination, ultrasonography and viral serology for Hepatitis A,B and C done also to rule out other causes of jaundice. Ultrasonography is done to assess the fetal well being, gestational age, amount of liquor, placental localization and any associated fetal anomalies. Alongwith that, their liver function tests including S. bilirubin, Alkaline phosphatase (ALT), serum transaminases (SGOT, SGPT) were also done. Serum fibrinogen levels, prothrombin time (PT), activated prothrombin time (APTT) were also measured in anticipation of bleeding episodes. Patients were hospitalized and for next forty eight to thirty six hours and were observed regarding worsening of symptoms.

These patients were treated in laison with physicians and anesthetist. If the gestational age was more than 28 weeks, neonatologists were also involved in anticipation for a preterm delivery. Patients were given intravenous infusions and their intake – out put was monitored. Antibiotics and life supportive drugs were started. A repeat investigations especially S. bilirubin, PT, S. fibrinogen and obstetrical scan were done after 48 hours to detect any early complication.

The anticipated maternal complications of acute viral hepatitis were observed. These complications are fever, oedema, ascites, paralytic illeus, nasal and gastro-intestinal haemorrhage, with clinical abnormal lab findings showing increased TLC (total leucocyte count), raised creatitine concentration, raised PT, APTT and serum fibrinogen levels. These patients also show fluid and electrolyte imbalance with hypoglycemia, hyponatriemia, hypokalemia and hypocalcemia. Anticipated obstetrical complications are antepartum haemorrhage (APH), post partum haemorrhage(PPH), preterm premature rupture of membrane (PPROM) and intra uterine death IUD. Those patients who showed worsening of disease either fetal or maternal were delivered (through operated or vaginal route). Those showing improvements of signs and symptoms and improved labs were managed conservatively or were sent home and managed on OPD basis.

Patients who developed fulminant hepatic failure (FHF) were managed in intensive care unit with supportive care. They received 20% mannitol, lactulose, antibiotics, parentenal invention and ventilatory support if and when needed.

Termination of pregnancy was done for fetal distress, intra-uterine growth retardation, intrauterine death or when gestational age was more than 37 weeks or when the bishop's score was favorable. Decision of operative delivery was again take for either present obstetrical complications like fetal distress, non-reactive CTG or reduced liquor and with H/O previous operative deliveries on the other hand, conservative management was done when the feto-maternal conditions were improving. Blood and fresh frozen plasmas were arranged to control ante or post partum bleeding.

Result

The study included only the pregnant patients presenting with jaundice and confirmed to have IgM or IgG Hepatitis E + ve and raised liver function test especially serum Bilirubin. The cut off value of serum bilirubin was 2mg/dl and above. A total of 33 patients were found with above sings and symptoms. It was observed that majority of patients i.e 18/33 were between 20 – 25 years old. These make up about 54% and out of the other remaining patient 10/33 were 26 – 30 years old (31%) and 5 patients (15%) were 31 years and above. As regards parity, 12/33 patients were primigravida and rest were G_2 or more showing ratio (36:63) gestational age as calculated from LMP (last menstrual period) or earliest scan showed age 7/33 patients were less than 28 weeks pregnant and rests of them were 28 weeks and more (26/33). Management was either conservative or interventional. Intervention was either done as induction of labour or Em. LSCS when there was worsening of symptoms or fetal distress. Fetal distress was diagnosed by Doppler study,

non-reactive cardiotorography (CTG) or reduced liquor on ultrasound. Monitoring of patients were done by repeating LFTs and coagulation profile twice weekly, CTG daily and obstetrical scan either weekly or twice weekly.

Patients with less than 28 weeks gestation when showed worsening of symptoms were given fresh frozen plasmas and induced but the fetal outcome was not measured due to non-probability of fetal viability. Fetal outcome in fetuses of more than 28 weeks gestation was measured with calculation of APGAR scores at 1 minute and 5 minutes intervals respectively and alive babies were followed up for another 1 weeks to observe for complications like jaundice, respiratory distress syndrome, asphyxia neonatorum or DIC. It was observed that 5 babies diagnosed to be dead in utero on first visit of patients and all of these were induced to attain vaginal delivery. Out of 21 patients, 14/21 had LSCS either due to fetal distress or due to worsening of maternal condition or due to her previous obstetrical history and 7/21 had SVD (LSCS 66% and SVD 33%).

Maternal morbidity and mortality was also observed and 10/33 patients developed worsening of symptoms. Out of these 10, 6 patients had DIC and 2 patients had PPH and 2 patients fulminant hepatic failure and expired. (6% maternal mortality).

Out of 21 patients with alive fetuses on admission. 16 babies delivered prematurely and had to be admitted in nursery. This shows high percentage i.e 61% of perinatal morbidity. Out of these 16 babies 5 babies expired in nursery within next 1 week i.e 10/26 showing a high perinatal mortality of 38% as a total of 10 babies expired (5 in utero and 5 after delivery).

Mode of delivery as mentioned earlier was either vaginal or lower segment caesarean section. Vaginal delivery was either spontaneous when patients developed labour pains naturally or labour was induced using medicines (PGE_1 and PGE_2). 14/33 patients i.e 42% has vaginal deliveries about 1/3rd patients were induced for labour. Induction of labour is itself a procedure associated with fetal distress and increased risk of operative delivery. As regards post partum hemorrhage and DIC, 2/4 had SVD and 2/4 had emergency LSCS. It has also observed that 2 patients developed fulmnant hepatic failure and both expired indicating a high risk condition.

Discussion

This study showed a younger age group trend for development of HEV infection during pregnancy. Hence more than 2/3rd of the patients were 30 years and below.[4] Similarly majority of patients were P1 – 3 i.e 75% again showing that younger age groups are affected more.[5] In consistent with a similar study, it is possible that as there is still a trend of early marriages in Pakistan and South – East Asia, the younger age group women are mostly affect. Secondly the habits of eating unclean, unhealthy and improperly cooked food among these pregnant women may be another cause of their condition.[4] Studies conducted in India, Ghana and other African countries show high prevalence of Hepatitis E in women with acute viral hepatitis in pregnancy.[2] Although the endemicity of the disease had not be reported by ministry of health or government officials but it has been observed so far that among pregnant women presenting with Hepatitis and jaundice, there is a high prevalence rate of Hepatitis E showing high rates of sub clinical infections in the country as also in a country like Ghana where the findings of higher HEV antibody prevalence among pregnant women. Ghana has poor sanitation and contamination of water supply country wide.[6,7] It was observed that majority of patients presented in 3rd trimester of pregnancy i.e 78% of patients presented with HEV + ve when they are 28 weeks or more pregnant. This is also similar to studies conducted previously in which more prevalence of Hepatitis E was found in 3rd trimester.[4,8,9]

As regards neonatal outcome, it was observed that on presentation, 15% of fetuses i.e 5/33 were received as intrauterine death (IUD) when the presented with viral E Hepatitis. At that time these women has high serum bilirubin levels and deranged liver function tests. This may indicate the chance of vertical transmission which may cause fetal death. Antepartum haemorrhage was also common again due to disturbances in coagulation profile. It was consistent with certain similar studies.[9] It was also observed that even in babies delivered alive and who were followed up in nursery, there was a high perinatal mortality of 47% and morbidity of 76%. The babies mostly suffered from complications of prematurity like respiratory distress syndrome (RDS), asphyxia neonatorum (ANN) and jaundice. This is similar to another study where 57/105 i.e 54% babies died in utero or within a week after delivery due to RDS and ANN.[10]

Poor maternal response to Hepatitis E can also be the result of prematurity, RDS and ANN in these either induction of labour or caesarean section was done due to worsening of signs and symptoms. It has

also been observed in several cross – sectional studies in which feto-maternal outcome in pregnancy due to Hepatitis A, B, C and E viruses were compared. It was also seen that incidence of fulminant Hepatitis failure was highest in patients suffering from Hepatitis E as compared to A, B, and C. In a study conducted in India where the cultural and socio-economic factors are comparable to our country, that out of 97 patients with acute viral hepatitis 47.4% had Hepatitis E. HEV was responsible for 36.2% of the cases of AVH and 75% cases of fulminant Hepatitis failure (FHF). 18/24 patients who expired were HEV + ve. Mortality rate was 39.1%.[11] Also studies among other researchers prove that Hepatitis E is the most common hepatotrophic virus associated with fulminant Hepatitis failure.[12] Considering conservative vs interventional approach. It has been observed that among pregnant patients, the decision to continue pregnancy with increasing levels of bilirubin and other liver functions tests, the mortality rate is high.[13] Hence conservative management or "wait see" policy should only be followed if the patients show signs of clinical and laboratory indices improvement.[14] Although no prophylaxis or vaccination has been developed so far for prevention of Hepatitis E with or without pregnancy but several studies show that antibody screening for Hepatitis E may be helpful during pregnancy in endemic areas.[15,16]

Although it may not be cost effective to screen antenatal patients and blood donors universally but at least Hepatitis E screening should be offered to such patients. This may prove helpful for the physician and the obstetrician to at protect these women against other nosocomIal infections and to ensure that newborns of Hepatitis E +ve mothers do not swallow maternal blood at the time of delivery in order to minimize perinatal HEV transmission.[9] Poor neonatal survival in Hepatitis E can not only be explained on preterm deliveries but also due to the fact that in a thickly populated and under developed country like Pakistan where there is high neonatal turn – over in nursery and the facilities are inadequate, may lead to high perinatal mortality. Similarly in a study conducted in India, it was observed that prematurity in HEV affected fetuses was as high as 84%.[17]

Maternal morbidity and mortality is also high in Hepatitis E +ve patients. Most of the women presented with acute viral Hepatitis 21/33 i.e 63.6% had acute viral Hepatitis with worsening of jaundice and abnormally raised LFTs. Out of these 6 patients developed medical complications like DIC, post partum haemorrhage and fulminant Hepatitis failure. However certain comparable studies show even higher maternal mortality and morbidity.[10] It has also been observed that there are variations in the findings regarding complications Hepatitis E among various researchers and different areas. There is a possibility that these studies may have smaller samples or may be done in times when there was an epidemic, one study shows 8% prevalence of HEV in Kashmir which seems quite high.[18]

In summary, it has been observed in this study and when the results compared with other related studies that Hepatitis E in pregnancy may have a worsening cause in pregnancy. It adversely affects both feto-maternal outcomes. In most of the circumstances, early delivery was decided due to worsening of maternal progress and that then leads to complications of prematurity in babies born to Hepatitis E +ve mothers.

Reference

1. Nicard E, Armstrong GL, Enouf V, Guthman JP, Gucrin JP, Caron M, Nizou JY, Andraghetti R: Genetic heterogeneity of hepatitis E in pDarfer, Sudan and neighbouring chard. J Med Viral 2005.
2. Khuroo MS. Study of an endemic 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.
3. Kraw zynski K, Aggarwal R, Kamili S. Hepatitis E infect Dis Clin North Am 2000.
4. Caro M, Kazanji M: Hepatitis E virus is highly prevalent among pregnant women in Gabon Central Africa with different patterns between rural and urban areas. Viral J 2008.
5. Aziz AB, Hamid S, Iqbal S, Islam W, Karim SA. Prevalence and severity of viral Hepatitis in Pakistani pregnant women. A five year hospital based study J Pak Med Assoc – 1997.
6. Emerson SU, Purcell RH: Hepatitis E virus. Rev. Med viral 2003.
7. Aggarwal R, Krawczynski K – Hepatitis: an overview and recent advances in clinical laboratory research. J Gastroentrol Hepatol 2000.
8. Purcell RH, Emerson SU: Hepatitis E. An emerging awareness of an old disease. J Hepatol 2008.
9. Weber JN, Tylor GP: Antenatal screening is important. BMJ 1996.
10. Patra S, Kumar A, Sagar ST, Puri M, Sarin SK. Maternal and fetal outcome in pregnant women with acute Hepatitis E virus infection. Inn int. Med 2007.
11. M Beniwal, A Kumar, P Kar, N Jilani, JB Sharma. Prevalence and severity of acute viral hepatitis and fulmi-

nant hepatitis during pregnancy. Ind J of Medical Microbiology 2003.
12. Jaiswal SPB Jain AK, Nak G, Soni N, Chitrus DS. Viral hepatitis during pregnancy Int. J Gynaec Obstet 2001.
13. Singh S, Mahanty A, Joshi YK, Dwivedi SN, Deka D. Outcome of Hep E virus infection in Indian pregnant women admitted to a tertiary care hospital. Indian J. Med Res. 2001.
14. Adijei AA, Tetty Y, Ayiyase JT, AduGyamli C, Obed S. Hep E virus infection is highly prevalent among pregnant women in Accra, Ghana. Virology Journal 2009.
15. Borhanmanesh F, Haghighi P, Hekmat K, Rezaizedeh K, Ghavani AG. Viral hepatitis during pregnancy. Severity and effect on gestation. Gastroentrol 1973.
16. Singh S, Mohanty A, Joshi YK, Deka D, Mohanty S, Panda SK: Mother – to – child transmission of hepatitis E virus infection Inj. J Paedrit 2003.
17. Kumar A, Beniwal M, Kav P, Sharma JB, Morthy NS: Hep E in pregnancy. Int J Gynecol Obstet. 2004.
18. Khuroo MS, Kamili S. Aetiology, clinical course and outcome of sporadic acute viral hepatitis in pregnancy. J viral Hepat. 2003.