ORIGINAL ARTICLE

MATERNAL & FOETAL OUTCOME IN PREGNANT LADIES HAVING ACUTE HEPATITIS E

Shahnaz Nadar[1], Muhammad Akbar Shah[2], Shahid Jamil[3], Hafsa Habib[3]
[1]Department of Gynae/Obs, and [3]Department of Medicine, Khyber Teaching Hospital, Peshawar, Pakistan

ABSTRACT

Background: Hepatitis E virus affects young people and females in the child bearing age. This study was conducted to determine the maternal & foetal outcome in pregnant ladies with acute hepatitis E.

Material & Methods: This cross sectional study was conducted at Khyber Teaching Hospital, Peshawar, from September 2013 to December 2014. Sixty patients with serologically proven evidence of acute hepatitis E virus infection and pregnancy admitted in gynecology & obstetrics ward and medical units were included in this study. All these patients were extensively studied and followed with liver function tests and coagulation profile. Maternal morbidity and mortality were recorded. After that maternal outcomes of these pregnancies were analyzed.

Results: Of the sixty cases, 5(8.3%) had miscarriages, 55(91.61%) were delivered, 39(65%) had preterm delivery and 16(26.66%) were delivered at term. Postpartum hemorrhage occurred in 18(30%), Disseminated intravascular coagulation 13(21.66%), Premature rupture of membranes 12(20%). Antepartum Hemorrhage 12(20%), vertical transmission took place in 20(33%) cases. Similarly acute liver failure occurred in 10(16.66%) patients. Maternal mortality took place in 16(26.66%).

Conclusion: Hepatitis E virus is major cause of acute hepatitis in women having pregnancy and having adverse maternal outcomes in these pregnancies.

KEY WORDS: Pregnancy; Acute hepatitis; Hepatitis E virus; Acute liver failure.

This article may be cited as: Nadar S, Shah MA, Jamil S, Habib H. Maternal & foetal outcome in pregnant ladies having acute hepatitis E. J Med Sci 2014; 13: 37-40.

INTRODUCTION

Hepatitis refers to parenchymal liver damage, with elevation of liver enzymes, if the duration of the illness is less than 6 months it's called acute hepatitis but if the duration of the illness is more than 6months it's called chronic hepatitis.[1] Acute hepatitis is most commonly caused by viral infection but non-viral agents like drugs, alcohol, poisons, mushroom, etc can also be the culprit.[2] Of viral causes A B C D E are very important. Acute hepatitis E is a type of viral hepatitis caused by hepatitis E virus.[3] Hepatitis E is probably the most common cause of acute hepatitis and jaundice in the world.[4]

Hepatitis E virus is non-enveloped positive sense, single stranded RNA virus that is 7.2 kb in length and contains three partially overlapping frame that are bracketed by short 5` and 3` non-translated regions.[5-7] Hepatitis E virus causes both outbreaks as well as sporadic cases of acute hepatitis throughout the world.[8] The outbreaks are more likely to occur in those countries which have limited resources, where there is limited access of peoples to the basic health services, clean and soft water, and proper clean sanitation and hygiene.[9]

Hepatitis E is predominantly transmitted through oro-fecal route by drinking contaminated water.[10] Apart from this route, other routes of transmission have also been identified which include food born transmission by ingesting the products derived from infected animals, transfusion of infected blood products, vertical transmission from pregnant women to their babies at the time of delivery, ingestion of raw and uncooked shellfish have also been implicated in the spread of sporadic cases.[11-13]

The illness caused by hepatitis E virus is characterized by acute onset just like those caused by other hepatotropic viruses and it is usually self-limiting in most of the cases.[14] However chronic form of hepatitis has also been reported in immune compromised people.[15] Typical clinical features of acute hepatitis E include anorexia, nausea, vomiting, asthenia, fatigability, lack of energy, fever, arthralgia, myalgia, generalized body aches and pain, abdominal pain, jaundice, right hypochondrial pain and tenderness, dark colored urine, pale stools, hepatomegaly and pruritus with excoriation of skin.[16]

Corresponding Author:
Dr. Shahnaz Nadar
Department of Gyne/Obs
Khyber Teaching Hospital
Peshawar, Pakistan
E-mail: shahnaz_nadar@yahoo.com

Acute hepatitis E is diagnosed by finding deranged LFTS (fivefold increase in alanine aminotransferase level) and positive IgM and IgG antibodies against Hepatitis E virus.[17] Though the disease is self-limiting in most of the cases, yet in some cases the illness is complicated by development of Acute Hepatic failure and other extra hepatic complications.[18] Acute Hepatitis E is particularly severe and dangerous in those ladies who are having pregnancy.[19]

Pregnant women with acute hepatitis E are at increased risk of various complications especially in their third trimester.[20] The mortality rate attributed to hepatitis E virus in women having pregnancy is 20-30% in various studies.[21-23] The various complications encountered in pregnant ladies and their babies are acute hepatic failure, acute renal failure, disseminated intravascular coagulation, multi organ failure, septicemia, preterm deliveries, antepartum hemorrhage, postpartum hemorrhage and death of women.[24] Various fetal complications have also been observed in hepatitis E virus positive mothers, which include increased fetal loss, intrauterine fetal death, premature rupture of membrane, premature birth of babies, hypoglycemia, icteric and anicteric acute hepatitis.[25] These complications are due to the fact that pregnant women transmit the viruses to their infants by vertical transmission at the time of delivery. At the moment there is no available treatment capable of eradicating the virus, only supportive measures are all that can be done. Hospitalization is necessary in those cases which are complicated by acute fulminant hepatic failure and other complications. Prevention is all that can be done effectively.

This study was conducted to determine the maternal & foetal outcome in pregnant ladies with acute hepatitis E.

MATERIAL AND METHODS

This cross-sectional descriptive study was carried out on pregnant ladies admitted in medical units as well as Gynecology and Obstetrical units of Khyber Teaching Hospital, Peshawar, from September 2013 to December 2014. Sample size was 60 by purtoxive sampling technique. Approval was taken from the Institutional Ethical Committee, pregnant ladies with serological and biochemical evidence of acute hepatitis E infection (HEV-IgM and IgG positive status) were included. Those having hepatitis caused by other viruses and other agents were excluded from the study.

Diagnosis of Acute Hepatitis E was made in those who were having clinical and biochemical evidence of acute hepatitis like jaundice, vomiting, anorexia and upper abdominal pain. All the routine tests were carried out like LFT, FBC, PT, APTT, serum albumin, urine R/E serum creatinine, blood urea and serum electrolytes, abdominal and pelvic ultrasound. These patients were investigated for cause of acute viral hepatitis by sending HBsAg, anti-HCV Antibodies, Anti-HAV IgM antibody, Anti-HEV IgM, and Anti-HEV IgG antibodies. All these patients were monitored in the hospital during their stay regarding their pregnancy status, whether continued or terminated.

All common complications whether obstetrical, medical or surgical were observed and noted. Maternal mortality was recorded, MMR was calculated, and data was analyzed on statistical software SPSS and expressed on descriptive statistic.

RESULTS

Sixty pregnant patients having hepatitis E were admitted in the hospital during the study period with mean age of 24.51$\pm$5.2 years. All these patients were having pregnancy of various gestational ages, most of the patients 35 (58.66 %) presented in their third trimester followed by 20 (33.3%) and 5 (8.3%) in second and first trimester respectively. Termination of pregnancy was carried out according to the gestational age.

All these Patients presented with clinical history of acute hepatitis like jaundice, anorexia, fever, malaise, nausea and vomiting. They were Anti-HEV IgM and IgG positive and were negative serological markers for other viruses like A, B, C and also no history of intake of hepatotoxic agents. Distribution of patients according to the clinical features revealed that 20 (33.33%) presented with altered sensorium and 52 (86.66%) with loss of appetite. Out of 60 patients 25 (66.66%) patients required intensive care support.

Out of 60 patients, 16 (26.67%) women died. Maternal mortality was 16 (26.67%) while 44 (73.33%) patients were discharged safely. Perinatal mortality rate was 30.3 per 1000 live births. Hemoglobin of these patients was 6-12 g/dl with mean value of 9.5$\pm$1.5 g/dl. Platelet count ranged 30-306 x10^9/L with mean of 157$\pm$82.4 x10^9/L. PT was between 10-60 Seconds with mean of 28.5$\pm$15.9. APTT ranged 22-80 with mean value of 44.22$\pm$20 Seconds. SGPT ranged 24-2080 with mean value of 605 IU/L.

Maximum derangement in hematological and biochemical profile was observed in those patients who presented during their 3rd trimesters. Acute fulminate hepatic failure occurred in 10 (16%) patients. Thirty-nine (65%) ladies had preterm deliveries and vertical transmission was seen in 20 (33%). Majority of patients presented during their third trimester of pregnancy 35 (58%) followed by second 20 (33.33%) and first trimester 5 (8.3%). (Fig. 1)

Various obstetrical complications were observed, of which postpartum hemorrhage (PPH) was

Table 1: Maternal outcome in pregnant ladies with acute hepatitis E (n=60)

Maternal Morbidity	Frequency	Percentage
Postpartum Hemorrhage	18	30
Disseminated intravascular coagulation	13	21.7
Premature Rupture of Membrane	12	20
Antepartum Hemorrhage	12	20
Miscarriage	5	8.3
Total	60	100

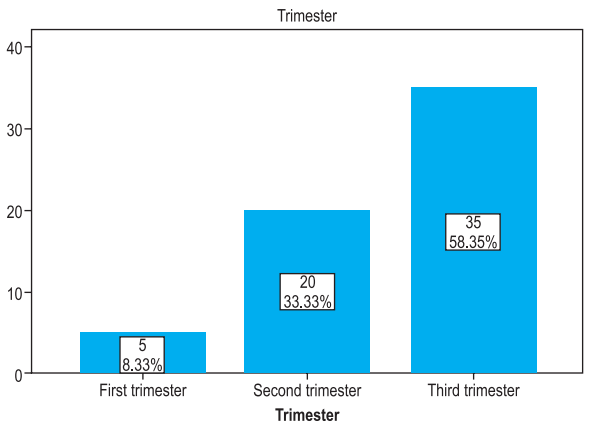

Figure 1: Distribution of acute hepatitis E among three trimesters of pregnancy.

the leading one, found in 18 (30%) patients followed by disseminated intravascular coagulation (DIC) in 13 (21.66%), antepartum hemorrhage and premature rupture of membranes in 12 (20%) patients. (Table 1)

DISSUSSION

Hepatitis E virus is an important cause of acute hepatitis, creating threat to pregnant ladies as pregnancy advances, especially in areas where safe drinking water is lacking. Hepatitis E virus affects young people and female in child bearing age of 18-45.

In our study we noticed that 70% of our patients were having age of 18-30years and 30% were in age range of 31-40%

Hepatitis E infection during pregnancy is associated with bad obstetrical events. We noticed that 65% of our patients had preterm deliveries between gestational age of 25-35 weeks. This observation is similar to that observed by Kumar et al[24] who said that 66% of women had preterm delivery.

The prevalence of hepatitis E infection increases with the gestational age. In our study we noticed that 58% and 33% of women presented during their third and second trimester respectively. Higher mortality and morbidity was noticed in those women who presented with higher gestational age. This observation correlates well with that observed by Jaiswal et al[27] who showed that 51% of women suffered in third trimester and developed various complications. Similarly Begum et al[28], in their study observed the fact that hepatitis E Virus affect most of the pregnant ladies in their third trimester followed by second and first trimester. Hepatitis E Virus infection during the pregnancy has got adverse prognosis especially in the third trimester as compared to second trimester.

In our study we observed that mortality rate of 26% in third trimester and 15% in second trimester. Kurrho et al[29] are also having similar observation that hepatitis E infection is more dangerous in third trimester than second trimester. The mortality rate in pregnant ladies affected by hepatitis E virus is 26% in our study which is also shown by Kumar et al[24] and Yasmeen et al.[22] Mortality occurred exclusively in those cases which were complicated by acute fulminant hepatic failure.

Acute hepatitis E infection during pregnancy is complicated by development of acute fulminant hepatic failure which is associated with very high mortality without liver transplantation. Acute fulminant hepatic failure took place in 16.66% patients in our study. All these patients were managed in intensive care unit and mortality in them was 93%. This observation was also seen by Daniel et al[30] who noticed that acute fulminant hepatic failure was associated with 85% mortality. The reason for high mortality in our study is that these patients required shifting to liver transplant center on urgent basis for liver transplantation which is the only curative treatment for acute fulminant hepatic failure. As no such center is available in our setup so these patients suffered a lot. Saeed et al[26] also noticed high mortality rate (50%) in patients with acute fulminant hepatic failure. However their sample size was too small.

Apart from these complications some other systemic complications also took place like consumption coagulopathy in 22%, antepartum hemorrhage in 20% and postpartum hemorrhage in 30% cases. These observations correlate with those by Kurrho et al[29], Kumar et al[24] and Yasmeen et al.[22] Small sample size is the main limitation of this study.

CONCLUSION

Hepatitis E is the major cause of acute hepatitis in pregnancy with unfavorable outcome both for mother and fetus.

We recommend appropriate preventive measures against HEV in pregnancy to reduce the

maternal and perinatal mortality in HEV endemic areas. Provision of safe drinking water is of utmost importance. Global voice should be raised to create vaccine against hepatitis E virus. More research should be delivered to find out exact pathogenesis of HEV in pregnancy and reasons for increased frequency of AHF in pregnancy.

REFERENCES

1. Kumar P, Clark M. Clinical Medicine. 8th edition. p. 316.
2. Walker BR, Colledge NR, Ralston SH, Penman ID. Anstee QM, Jones DEJ. Davidson's Principles and Practice of Medicine. 22nd edition. p. 948.
3. Freedman LS. Liver, Biliary Tract and Pancreas Disorders. In: Papadakis MA, McPhee SJ. Current Medical Diagnosis and Treatment. McGraw Hill Education, Lange Medical Publication. 54th Edn, New York, USA. 2015. p. 658-715.
4. Kamar N, Bendall R, Legrand-Abravanel F, Xia NS, Ijaz S, Izopet J, et al. Hepatitis E. Lancet 2012; 379:2477-88.
5. Hoofnagle JH, Nelson KE, Purcell RH. Hepatitis E. N Engl J Med 2012; 367:1237-44.
6. Guua TSY, Liub Z, Yea Q, Mataa DA, Lic K, Yinb C, et al. Structure of the hepatitis E virus-like particle suggests mechanisms for virus assembly and receptor binding. PNAS 2009; 106:12992-7
7. Xing L, Li TC, Mayazaki N, Simon MN, Wall JS, Moore M, et al. Structure of hepatitis E virion-sized particle reveals an RNA-dependent viral assembly pathway. J Biol Chem 2010; 285:33175–83.
8. Albetkova A, Drobeniuc J, Yashina T, Musabaev E, Robertson B, Nainan O. Characterization of hepatitis E virus from outbreak and sporadic cases in Turkmenistan. J Med Virol 2007; 79:1696-702.
9. Tsega E, Krawczynski K, Hansson BG, Nordenfelt E, Negusse Y, Alemu W, et al. Outbreak of acute hepatitis E virus infection among military personnel in northern Ethiopia. J Med Virol 1991; 34:232-6.
10. Suzuki K, Aikawa T, Okamoto H. Fulminant hepatitis E in Japan. N Engl J Med 2002; 347:1456
11. Robson SC, Adams S, Brink N, Woodruff B, Bradley D. Hospital outbreak of hepatitis E. Lancet 1992; 339:1424-5.
12. Khuroo MS, Kamili S, Jameel. Vertical transmission of hepatitis E. Lancet 1995; 345:1025-6.
13. Psichogiou M, Tzala E, Boletis J, Zakopoulou N, Loutradi A, Maliori M, et al. Hepatitis E virus infection in individuals at high risk of transmission of non-A, non-B hepatitis and sexually transmitted diseases. Scand J Infect Dis 1996; 28:443-5.
14. Navaneethan U, Al-Mohajer M, Shata MT. Hepatitis E and pregnancy - understanding the pathogenesis. Liver Int 2008; 28:1190-9
15. Kamar N, Selves J, Mansuy JM, Ouezzani L, Péron JM, Guitard J, et al. Hepatitis E virus and chronic hepatitis in organ-transplant recipients. N Engl J Med 2008; 358:811-7.
16. Aggarwal R. Hepatitis E: the endemic perspective. Clin Liver Dis 2013; 2:240-4.
17. Mónica V, António F, Helena G, Ana M, Elia M, Zélia N, et al. Fulminant hepatitis E in a pregnant woman. GE J Port Gastrenterol 2013; 20:210-4.
18. Banait VS, Sandur V, Parikh F, Murugesh M, Ranka R, Ramesh VS, et al. Outcome of acute liver failure due to acute hepatitis E in pregnant women. Indian J Gastroenterol 2007; 26:
19. Goumba CM, Yandoko-Nakouné ER, Komas NP. A fetal case of acute hepatitis E among pregnant women, Central African Republic. BMC Res Notes 2010; 3:103
20. Tsega E, Hansson BG, Krawczynski K, Nordenfelt E. Acute sporadic viral hepatitis in Ethiopia: causes, risk factors, and effects on pregnancy. Clin Infect Dis 1992; 14:961-5.
21. Sultana R, Humayun S. Fetomaternal outcome in acute hepatitis E. J Coll Physicians Surg Pak 2014; 24:127-30.
22. Yasmeen T, Hashmi HA, Taj A. Fetomarnal outcome with hepatitis E in pregnany. J Coll Physian Surg Pak 2013; 23:711-4
23. Rayis DA, Jumaa AM, Gasim GI, Karsany. An outbreak of hepatitis E and high maternal mortality at Port Sudan, Eastern Sudan. Pathog Glob Health 2013; 107:66-8.
24. Kumar A, Patra S, 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.
25. Aggarwal R. Clinical presentation of hepatitis E. Virus Res 2011; 161:15-22.
26. Saeed S, Hamid SM, Jafri W, Khan H, Shah H. Fulminant hepatic failure in pregnant women: acute fatty liver or acute viral hepatitis. J Hepatol 1996; 25:20-7.
27. Jaiswal SP, Jain AK, Naik G, Soni N, Chitnis DS. Viral hepatitis during pregnancy. Int J Gynecol Obstet 2001; 72:103-8.
28. Begum N, Polipalli SK, Hssain SA, Kumar A, Kar P. Duration of hepatitis viremia in pregnancy. Int J Gynaecol Obstet 2010; 108;207-10
29. Kuhroo MS, Kamili S. Aetiology, clinical course and outcome of sporadic acute viral hepatitis in pregnancy. J Viral Hepat 2003; 10:61-9.
30. Gotthardt D, Riediger C, Weiss KH, Encke J, Schemmer P, Schmidt J, et al. Fulminant hepatic failure: etiology and indications for liver transplantation. Nephrol Dial Transplant 2007; 22:5-8.

CONFLICT OF INTEREST
Authors declare no conflict of interest.
GRANT SUPPORT AND FINANCIAL DISCLOSURE
None declared.