ORIGINAL ARTICLE

Fetomaternal Outcome in Acute Hepatitis E

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Abstract

Objective: To determine fetomaternal outcome in pregnant women with acute hepatitis E in terms of pregnancy outcome and perinatal mortality.

Study Design: Case series.

Place and Duration of Study: Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital, Lahore, from July 2012 to March 2013.

Methodology: Serum samples of 38 patients who presented with jaundice in pregnancy were collected to detect hepatitis E IgM antibodies. Demographics, pregnancy outcome and perinatal mortality was noted in hepatitis E positive cases with cause of complications. Cases with jaundice due solely to any other cause were excluded.

Results: Twenty five patients had acute hepatitis E with coexistent acute hepatitis A in 1(4%) patient. Their mean age was 25 years and mean gravidity was 2. Among them, 10 (40%) patients were primigravida followed by gravida two in 7 (28%) cases. Twenty four (96%) patients presented in third trimester of pregnancy and in 1 (4%) pregnancy ended in second trimester missed miscarriage. The mean gestational age was 32 weeks. Twenty one (84%) babies were born alive, among them 18 (86%) were preterm. Perinatal mortality was 26%; contributed by intrauterine deaths and early neonatal deaths in 3 (14%) cases each. Total maternal deaths were 5 (20%), 4 (80%) in postpartum period and 1 (20%) in antepartum period due to fulminant hepatic failure in all cases.

Conclusion: Prematurity in newborns and fulminant hepatic failure in mothers are major cause of poor fetomaternal outcome in acute hepatitis E in pregnancy.

Key Words: *Pregnancy. Acute hepatitis E. Fetomaternal outcome. Prematurity. Fulminant hepatic failure.*

INTRODUCTION

Hepatitis E is a global health problem. It is an acute self-limiting viral liver infection. The hepatitis E virus infection was first differentiated as a separate disease from hepatitis A virus during water born epidemic of acute hepatitis in Kashmir, India in 1980.[1,2] Hepatitis E is caused by a small non- enveloped single stranded RNA virus. The virus has four genotypes and one serotype. Genotypes 1 and 2 predominantly infect humans. Large outbreaks in developing countries are usually caused by genotype 1.[3] Hepatitis E is primarily transmitted through feco- oral route; other routes of its transmission are vertical, parenteral and nosocomial.[4] The disease usually affects young adults. It may present as out-breaks in areas of poor sanitation and also as sporadic cases with acute self-limiting hepatitis.[5]

Incidence, morbidity and mortality of hepatitis E are high in pregnancy. It is due to hormonal and immunological changes occurring in pregnancy. The raised levels of estrogen, progestogen and human chorionic gonado-tropin in pregnancy have suppressive effect on the cell mediated immunity and also promote viral replication.[6] It may take severe course in patients with chronic liver disease, HIV and organ transplant recipient.[7,8] Pregnant women with acute hepatitis E infection have 15% risk of fulminant liver failure leading to maternal death in 20% cases. Fulminant hepatic failure is specifically common in pregnant Asian females. It is due to high HEV exposure and low immune status of Asian pregnant women. Another contributory factor is folic acid deficiency which is common in Asian pregnant females. The timely intervention and pregnancy termination is the only treatment option along with supportive care.[9,10]

An understanding of disease complications can help to formulate effective strategies for disease prevention, control and patient management leading to better fetomaternal outcome.

The aim of this study was to determine the fetomaternal morbidity and mortality associated with hepatitis E virus infection during pregnancy.

METHODOLOGY

This case series was conducted in the Department of Obstetrics and Gynecology of Sir Ganga Ram Hospital, Lahore, from July 2012 to March 2013. It was reviewed and approved by Ethical Review Board of Fatima Jinnah Medical College / Sir Ganga Ram Hospital, Lahore. Initially, all patients presented with jaundice in pregnancy were enrolled. Later on, only those cases that were diagnosed as acute hepatits E were includued in

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the study. 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 and non-pregnant patients with jaundice were excluded from the study.

Serum samples of 38 patients who presented with jaundice in pregnancy were collected and sent to laboratory for detection of hepatitis E IgM antibodies. Viral serology for hepatitis A, B and C was also done to rule out other causes. Data was collected after an informed consent from 25 patients who fulfilled the inclusion criteria. Relevant information was collected on especially designed proforma. It included age of patient, gravidity, residential area, gestational age and fetomaternal outcome. 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. Neonates were followed till first week of their life.

Data analysis was computer based. Data entry sheet was designed in computer software SPSS version 14 and analyzed. Variables of interest were age, gravidity, residential area, gestational age at presentation, fetal and maternal outcome etc. Quantitative variables such as age, gravidity and gestational age were analyzed using simple descriptive statistics like mean and standard deviation. Qualitative variables such as residential area, fetal and maternal outcome were calculated using frequency and percentage.

RESULTS

The serology for hepatitis E revealed that 25 patients had acute hepatitis E with co-existent acute hepatitis A in 1 (4%) of the patients. Hepatitis A IgG antibodies were positive in 3 (12%) patients with acute hepatitis E. The distribution of cases according to residential area is shown in Figure 1. Age, gravidity and gestational age of patients at presentation is shown in Table I. Ten (40%) patients were primigravida followed by gravida two in 7 (28%) cases and 8 (32%) patients were gravida 3 or more.

Fetal outcome in patients infected with acute hepatitis E in pregnancy is shown in Figure 2. Among 21 alive babies, 3 (14%) were born at term and 18 (86%) were preterm. Among preterm babies, 10 (56%) were mildly preterm, 6 (33%) moderately preterm and 2 (11%) were extremely preterm. All newborns were followed till first week of their life. Out of 18 preterm babies, 14 suffered from complications of prematurity like respiratory distress syndrome in 5 (36%), asphyxia neonatorum in 4 (28%) and jaundice in 5 (36%) cases. Three babies expired during early neonatal period, 2 (67%) due to respiratory distress syndrome and 1 (33%) due to asphyxia neonatorum.

There were 24 (96%) patients who presented in third trimester and in 1 (4%) female pregnancy ended in second trimester missed miscarriage. Out of the 24 patients, mode of delivery was vaginal in 18 (75%) cases and caesarean section was carried out in 6 (25%) patients due to obstetric indications. Labour was induced using prostaglandin E1 or E2 in 10 (55.6%) cases while 8 (44.4%) patients had spontaneous labour leading to vaginal delivery. Induction of labour was done due to worsening of maternal condition in 7 (70%) patients and due to intra-uterine deaths in 3 (30%) cases. Indications of lower segment caesarean section were primi-breech in 2 (33%) patients, scarred uterus in 2 (33%), failure to progress in 1 (17%) and fetal distress in 1 (17%) patient.

Twenty patients (80%) recovered from acute illness. There were 5 (20%) maternal deaths. In 4 (80%) cases, maternal deaths occurred in postpartum period and 1 (20%) patient died in antepartum period. All maternal mortalities were due to fulminant hepatic failure.

Table I: Descriptive variables.

	N	Minimum	Maximum	Mean	Std. Deviation
Age (years)	25	19.00	30.00	25.00	3.426
Gravidity (No.)	25	1.00	5.00	2.24	1.36
Gestation (weeks)	25	16.00	40.00	32.00	5.02

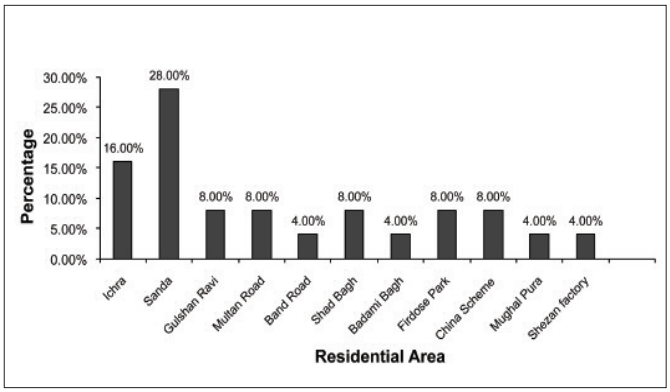

Figure 1: Case distribution according to residential area.

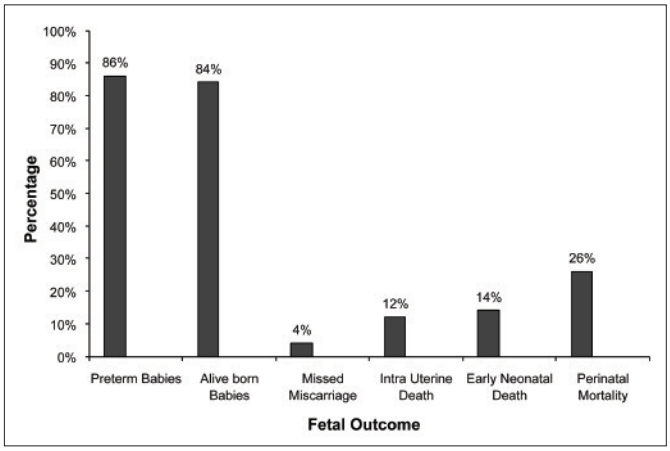

Figure 2: Fetal outcome in pregnant patients with acute hepatitis E.

DISCUSSION

Hepatitis E is the most frequent cause of non-A, non-B enterically transmitted acute viral hepatitis in developing countries.[11] Pakistan has a high disease burden of hepatitis A to E with high morbidity and mortality. A number of mini-epidemics have been reported in Pakistan. Lack of specific risk factors for sporadic hepatitis E makes it difficult to develop preventive strategies.

A large number of patients with acute hepatitis E had co-infection with hepatitis A. It can be due to common route of viral transmission for hepatitis A and E.[12]

The highest sero-prevalence rates of hepatitis E are observed in regions with low standards of sanitation.[12] Geographical distribution in present study revealed a very interesting fact that more than half of the patients were from low-resource setting areas. Attention of authorities should be drawn towards these areas of high prevalence for identification of underlying factors.

Mean maternal age of our patients was 25 years. In 40% of cases patients were primigravida. These findings are consistent with the study conducted by Shrestha *et al*. which revealed that 45% patients with acute hepatitis E were primigravida.[13] Acute hepatitis E commonly affects pregnant females. The younger age group is mostly affected due to trend of early marriages in South East Asia.

Hepatitis E virus infection is more common in third trimester of pregnancy. Mean gestational age at presentation was 32 weeks in present study. The same is reported by Shrestha *et al*.[13] A study conducted in Sudan reported a relatively smaller gestational age (28 weeks).[14] This variation may be due to regional differences.

Perinatal mortality and morbidity is significantly high in patients infected with acute hepatitis E, mainly contributed by complications of prematurity. The present study revealed 26% perinatal mortality. Similar observation was made from Nepal.[13] Mansoor *et al*. also reported a poor perinatal outcome with 38% perinatal mortality.[15] They identified that babies mostly suffer from complications of prematurity, like respiratory distress syndrome, asphyxia neonatorum and jaundice. The incidence of prematurity in general population is 4 - 12%.[16] It was observed that 86% babies were preterm in this study. Similar results were observed in various studies that acute hepatitis E is associated with increased risk of prematurity.[15] It is due to the fact that acute hepatitis E infection is more common in the third trimester of pregnancy and deteriorating maternal condition warranting pregnancy termination resulting in premature births.

The number of maternal deaths is significantly high in patients with acute hepatitis E due to fulminant hepatic failure and coagulation failure. In the present study, maternal mortality was 20% and cause of death was fulminant hepatic failure in all cases. Shrestha *et al*. observed that in patients with acute hepatitis E, three quarters of maternal mortalities were due to fulminant hepatic failure.[13] In majority of cases condition of the patients deteriorated after delivery and mortality occurred in postpartum period. This observation can partly be explained by the fact that process of multi-organ failure has been already initiated in antepartum period. However, exact underlying mechanism for this deterioration is not yet clear.

Hepatitis E mainly spreads by water contaminated with human fecal matter. The risk of infection and transmission can be reduced by providing quality standards for public water supplies. Measures should be taken to establish proper disposal system to eliminate contamination of drinking water. Serology screening in susceptible areas should be ensured. Community awareness should be created at mass level to observe and maintain hygienic practices in daily life.[17] According to World Health Organization, cases of hepatitis declined after implementation of hygienic and water chlorination measures in endemic areas.[18]

Vaccination is an important step in disease prevention. The world's first hepatitis E vaccine, Hecolin was approved by China's State Food and Drug Administration (SFDA) in December 2011 after a phase-III clinical trial published in 2010. Data suggests that it was highly effective in preventing infection in 1,1165 healthy participants. Now it is commercially available in China. Xiamen University of China is collaborating with World Health Organization to make it available globally.[19,20] Programs for safe and effective hepatitis E vaccination should be launched for prompt disease prevention and control.

Disease burden can substantially be reduced by employing preventive strategies. An awareness campaign regarding hygienic practices in daily life, safe disposal of human waste, provision of clean water and vaccination can sensitize the public and improve the situation.

CONCLUSION

Acute hepatitis E in pregnancy had a poor fetomaternal outcome. Deteriorating maternal condition warranting pregnancy termination resulting in premature births is major cause of adverse neonatal outcome. All maternal deaths occurred due to fulminant hepatic failure.

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