Original Article

Fulminant Hepatic Failure in Pregnancy and its Association with Viral Hepatitis E

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ABSTRACT

Objective: To determine the frequency of fulminant hepatic failure in pregnancy and its association with viral hepatitis E.

Study Design: A retrospective study

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Liaquat Medical University Hospital, Hyderabad, from April 2019 to April 2021 for a period of two years.

Materials and Methods: One hundred fulminant hepatic failure pregnant ladies were enrolled. Main variables of study were gestational age, duration of disease, IgM (positive/negative) for hepatitis E virus, maternal complications and mortality. Statistical package for social sciences version 23 was used for data analysis. Mean and standard deviation for numerical data like age and gestational age and frequency and percentages for categorical data like IgM (positive/negative).

Results: The mean age, gestational age of patients and duration of disease were 26.25±4.87 years, 31.16±3.82 weeks and 2.45±1.14 weeks respectively. Most of the patients had 3 or more weeks of disease. Number of patients n=61 (61.0%) were found to be IgM positive for the hepatitis E virus. Maternal mortality was noted as n=71 (71.0%) and live births were 41 (41.0%). No association was found between age, gestational age and duration of disease (P-value, 0.364, 0.107 and 0.956 respectively).

Conclusion: Hepatitis E infection during third trimester of pregnancy can leads to fulminant hepatic failure and associated with number of fetal and maternal complications. Special prevention plan is necessary along with awareness and public health facilities. Timely diagnosis especially IgM anti HEV is mandatory.

Key Words: Fulminant Hepatic Failure, Hepatitis E virus, Maternal complications, Pregnancy

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INTRODUCTION

ALF, acute liver failure is a rare clinical syndrome. It is described as abrupt and extensive hepatic necrosis in a healthy liver without any prior disease, which culminate in jaundice, hepatic encephalopathy and coagulopathy (INR>1.5)[1]. It can be sub-fulminant or fulminant hepatic failure (FHF); both are described by progression of hepatic encephalopathy following the emergence of critical liver disease.

The difference between Sub-fulminant and fulminant hepatic failure is characterized by the time of emergence of symptoms; in former it is between 8 weeks and 6 months of liver disease and in later within 8 weeks[2].

There is little chance of recovery in both cases but there is a hope of reversal and recovery towards normal health life. Hepatitis E virus (HEV) is a small quasi-enveloped, single-stranded RNA virus. Its incubation period is between two and nine weeks. Its transmission occurred through feco-oral route[3]. In parts of Asia, Africa, the Middle East and Central America this virus is believed to be of endemic scale, where sizeable outbreaks occur due to insufficient hygiene and water-borne diseases. HEV Genotype 1 is hyper-endemic in Asia and Africa, which causes the following conditions of sporadic acute hepatitis, acute or chronic hepatic failure and acute hepatic failure[4]. HEV Genotype 2, also causes same ailments, is found in Mexico and Nigeria. HEV Genotypes 3 and 4 are predominant in the developed nations[5].

Humans are thought to be primary reservoir of HEV genotype 1 and 2 and for HEV genotype 3 and 4 pigs are considered as primary reservoirs, therefore zoonotic transmission is a common occurrence[6]. While HEV genotypes 3 and 4 have not been found associated with severe liver disease but further research is required to validate this observation. Hepatitis E causes serious problems in pregnant women[7].

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FHF in pregnant women due to HEV is a severe condition with symptoms such a short pre-encephalopathy period; consumptive coagulopathy also known as disseminated intravascular coagulation and rapid development of cerebral edema[8]. Pregnant women with HEV related acute hepatitis have unfortunate maternal and fetal results. A study in India done and reported that 81% of cases of fulminant hepatic failure during pregnancy were due to hepatitis E virus[9,10].

The main aim of this investigation is to seek out independent validation of high rate of fulminant hepatic failure caused by Hepatitis E virus during pregnancy in our region and to estimate the related mortality and morbidity.

MATERIALS AND METHODS

Study was carried out at department of Obstetrics & Gynecology, Liaquat Medical University Hospital, Hyderabad, from April 2019 to April 2021 in two years duration. This was a retrospective Study. Ethical approval was taken from hospital ethical board. Informed written consent was obtained from patient after detailed information. Patients presented with FHF during antenatal period were enrolled in study. Pregnant women with age below forty years and 3 months gestational amenorrhea were included in the study. Hepatic failure presented as hepatic encephalopathy, jaundice and coagulopathy (INR below 1.5) were labeled as fulminant hepatic failure.

Complete physical examination was done in all patients and complete blood count, liver function test, urine complete examination, serum urea and creatinine, ultrasonography of abdomen and pelvis were done. Viral serology with IgM for hepatitis E virus was calculated. Patients with known cardiac disease, eclampsia, pre-eclampsia and chronic liver failure were excluded from the study. Antibiotic treatment (Ceftriaxone) was administered to all patients.

Patient's data was entered in SPSS version 23 for data analysis and mean ± SD was calculated for numerical variables like age, gestational and frequency and percentages were calculated for categorical data like hepatitis E. Test of significance were applied to see association among variables. P Value less than or equal to 0.05 was considered as significant.

RESULTS

One hundred three fulminant hepatic failure patients were included in this study. The mean age of the patients was 26.25±4.87years. Majority of the patients were between 26-35 years. The mean gestational age of the patients was 31.16±3.82 weeks. The mean duration of disease was 2.45±1.14 weeks. Most of the patients had 3 or more weeks of disease. n=61 (61.0%) patients were found to be IgM positive for the hepatitis E virus. (Table. I).

There was no association between IgM and age, gestational age and duration of disease. (Table. 2).

Table No.1: Demographic variables of the patients

Variable	N (%)
Age distribution (years)	
18-25	46 (46.0)
26-35	49 (49.0)
36-45	5 (5.0)
Gestational age (weeks)	
25-28	28 (28.0)
29-31	36 (36.0)
32-37	29 (29.0)
38-45	7 (7.0)
Duration of disease (weeks)	
1	22 (22.0)
2	35 (35.0)
3 or more	43 (43.0)
IgM	
Positive	61 (61.0)
Negative	39 (39.0)
Parity	
Primi	71 (71.0)
G2	19 (19.0)
G3 or more	10 (10.0)

Table No.2: Association of IgM with independent variables

Variable	Category	IgM		P-value
		Positive	Negative	
Age distribution (years)	18-25	31	15	0.364
	26-35	28	21	
	36-45	2	3	
Gestational age (weeks)	25-28	14	14	0.107
	29-31	23	13	
	32-37	17	12	
	38-45	7	0	
Duration of disease (weeks)	1	13	9	0.956
	2	22	13	
	3 or more	26	17	

Table No.3: Maternal mortality and other complications of the patients

Complication	N (%)
Second trimester	24 (24.0)
Third trimester	76 (76.0)
Hepatic encephalopathy	14 (14.0)
Gastrointestinal hemorrhage	12 (12.0)
Ascites	69 (69.0)
Renal failure	29 (29.0)
Coagulation defeat	41 (41.0)
ICU admission	17 (17.0)
Transfusion (blood/blood products)	38 (38.0)
Mortality	71 (71.0)

Maternal mortality was noted as n=71 (71.0%). Medical complications presented in table 3. There was n=26 (26.0%) IUD and spontaneous abortions. Still births were 26 (26.0%) and live births were 41 (41.0%). Fetal outcomes were shown in table. 4.

Table No.4: Fetal outcomes of the patients

Outcome	N (%)
IUD	26 (26.0)
Spontaneous abortions	2 (2.0)
Preterm babies	68 (79.1)
Still birth	26 (26.0)
Live birth	41 (41.0)
Neonatal death	71 (71.0)
Low birth weight	47 (54.7)
Meconium stained liquor	6 (7.0)
NICU admissions	27 (31.4)

DISCUSSION

During pregnancy complication may arise due to severe liver issues including hepatic failure. As some liver disorders are particular to pregnancy, AFLP (acute fatty liver of pregnancy) and HELLP syndrome are rare, whereas obstetric cholestasis and liver dysfunction associated with preeclampsia are common[11]. Some hepato-biliary disorders are cause of concern as they are more expected to occur during pregnancy and can cause serious damage, like gall stones and hepatic vein thrombosis and acute hepatitis E[12].

Hepatitis E virus is one of the major causes of fulminant hepatic failure in pregnant women. Its occurrence during pregnancy is sudden and severe; the results are often fatal. About 20% of pregnant women are infected with viral fulminant hepatitis; out of which 20% of women die during the third trimester of pregnancy[13]. Furthermore, it increases the risk of fetal complications and fetal death. At the moment there is no antiviral medicine or vaccine available for HEV, though some trials are undergoing for the development of vaccines[14].

In our research, out of n=100 pregnant women suffering from fulminant hepatic failure 61 (61%) were infected with HEV. This result agrees with the following studies conducted by Jaiswal et al[15] in India, Al-Mahtab et al[16] in Dhaka and Khuroo et al[13] where they found HEV to be in 57.5%, 56.52% and 61.8% of the FHF cases respectively.

However, Kumar A et al[17] recorded 81% of FHF cases due to HEV. This dissimilarity is perhaps due to the following factors; they included all jaundice patients during pregnancy and did not exclude patients with co morbid diseases. Moreover, their sample size was smaller in comparison. About 80% of our studied patients were 20 to 34 years of age group. This observation matches with Shrestha et al[18] from Nepal; their 76% of patients were in this age group. We observed 61% of women were between 29 to 42 gestational weeks. Yuel et al[19] in India observed similar pattern with 52% of women.

We observed maternal mortality due to HEV in 71% of the cases. Higher results regarding mortality in Bangladesh was 80% in hepatitis E patients associated with FHF reported by Mamun-Al-Mahtab et al[20]. It is probably due to the fact that we excluded the patients with chronic liver diseases or other comorbidities. Most of our patients were less than 35 years; Survivability chances decreases with advancement of age. Timely administration of broad spectrum antibiotics has been related to decrease in mortality rate of FHF patients[21].

A study was conducted by Brohi et al[22] and reported that fulminant hepatic failure and its association with pregnancy is a huge clinical issue that can be recovered with early diagnosis and treatment. We administered antibiotics of Ceftriaxone in all of our patients, which could have resulted in low mortality[23]. However, we cannot validate this conclusion since no parallel group of patients existed to which no antibiotics were administered.

It is imperative that HEV associated diseases should be taken seriously owing to its worldwide existence, an effective vaccine with long term immunity is immediately needed. This necessitates the responsiveness of public health scientists, academia and the health authorities. It is a need of hour to reduce the morbidity and mortality caused by HEV.

CONCLUSION

Hepatitis E infection during third trimester of pregnancy can leads to fulminant hepatic failure and associated with number of fetal and maternal complications. Special prevention plan is necessary along with awareness and public health facilities. Timely diagnosis especially IgM anti HEV is mandatory.

Recommendations: There is need for further studies on comparison of fetomaternal outcomes and women diagnosed with hepatitis E during pregnancy and its complications associated with liver injury. Conclusion of this study will be helpful in selection of more precise treatment plan of hepatitis E patients in acute phase of disease. Studies of this type are highly recommended in obstetrical research.

Author's Contribution:

Concept & Design of Study:	Fahmida Parveen Memon
Drafting:	Sakeena Ahmed Memon, Almas
Data Analysis:	Almas, Shahla Afsheen
Revisiting Critically:	Fahmida Parveen Memon, Sakeena Ahmed Memon
Final Approval of version:	Fahmida Parveen Memon

Conflict of Interest: The study has no conflict of interest to declare by any author.

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