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HEPATITIS E ASSOCIATED FULMINANT HEPATIC FAILURE AND ITS OUTCOME IN PREGNANCY.

Zahida Parveen Brohi[1], Uzma Parveen[2], Aneela Sadaf[3]

1. MBBS, FCPS
Associate Professor Obstetrics & Gynecology
Bilawal Medical College for Boys (LUMHS).
Jamshoro Sindh, Pakistan.
2. MBBS, FCPS
Assistant Professor Obstetrics & Gynecology
Isra University Hospital Hyderabad Sindh, Pakistan.
3. MBBS, MS (Gynecologist)
Gynecologist Obstetrics & Gynecology
Services Hospital Karachi Sindh, Pakistan.

Correspondence Address:
Dr. Zahida Parveen Brohi
Department of Obstetrics & Gynecology
Bilawal Medical College for Boys (LUMHS)
Jamshoro Sindh, Pakistan.
zahidaparveen66@yahoo.com

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ABSTRACT… Objectives: To determine the clinical features and outcome of hepatitis E associated fulminant hepatic failure in pregnancy. **Study Design:** Observational Retrospective study. **Setting:** Department of Obstetrics & Gynecology at Isra University Hospital Hyderabad. **Period:** Three years from 1st January 2015 to 31st December 2017. **Material & Methods:** Total 3596 obstetric patients were admitted whom 168 pregnant women who were positive for hepatitis E viral marker have been included in the study. **Results:** Their age was between 18 to 47 years with mean age 26.04±6.40 years; majority of patients had not received antenatal care 123 (73.2%). Out of 168, 27 (16%) presented in the first trimester, 45 (26.7%) presented in the second trimester, while 96 (57.1%) patients developed fulminant hepatic failure in their 3rd trimester of pregnancy. Out of 168, 111(66%) patients delivered and 57 (33.9%) were undelivered. Fetal and perinatal outcome of delivered patients showed miscarriage 45 (40.5%), stillborn 25(14.8%), preterm delivery 17(15.3%), neonatal death 7 (6.3%) and 17 (15.3%) new born remained alive. Overall maternal mortality was 51 (30.3%). **Conclusion:** Hepatitis – E related fulminant hepatic failure in pregnancy is a troublesome clinical issue and connected with exceptionally high maternal and fetal mortality. Appropriate diagnosis, early timely intervention can considerably diminish the morbidity and mortality associated with (HEV) Fulminant hepatic failure.

Key words: Fulminant Hepatic Failure, Mortality, Pregnancy.

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INTRODUCTION

Hepatitis E is inflammation of liver caused by hepatitis E virus which is a positive strand RNA virus transmitted principally through the fecal-oral route; it is the most frequent reason of fulminant hepatic failure in prevalent areas.[1] Disease arise in the variety of major epidemics linked to contamination of water supplies or within the form of infrequent cases in the absence of apparent disease[2] "acute viral hepatitis globally associated with likely 20 million cases of HEV infection and 70 000 deaths/year.[3] In men and non-pregnant ladies, the disease is normally self-constrained and has a low death rate 0.1 %.[4]

Pregnant females especially from the third world countries are at greater risk of having acute HEV infection and resulting grave complications including acute liver failure with very sky high maternal and fetal morbidity and mortality.[1]

A changed condition of hormones and immunity are seen during pregnancy yet the genuine reason for high mortality is not known, however It is likely that poor nutrition and pregnancy would be a possible risk factor for viral multiplication and lower immunity in Indian/Asian pregnant ladies.[5] It is proposed that reduced cellular immunity (indicated by a decrease in CD4, an increase in CD8 cell counts and lowered CD4/CD8 cell ratio) and an elevated level of steroid hormones that impact viral replication during pregnancy and possible cause of severe illness.[5]

High fetal mortality could be due to in-utero foetal transmission of hepatitis-E virus results in fetal hepatitis.[6]

It might associated with maternal and fetal complications including abortion, intrauterine fetal death, preterm labor and maternal or neonatal death.[1,7,8]

These patients were referred from remote areas in very late stages, In spite of freely available screening and diagnostic tests for viral hepatitis every patient could not meet the expense of due to their high cost, so there is reluctance for tests in peripheral areas further hold up the diagnosis as well as referral to tertiary care units and results in increased morbidity as well as mortality. The aim of this research was to determine the maternal and fetal effect of Fulminant hepatic failure in pregnancy in our population.

MATERIAL & METHODS

This retrospective observational study was conducted in the Obstetrics and Gynecology department of Isra university Hospital Hyderabad Sindh for the three years from 1st January 2015 to 31st December 2017.

A Total 168 pregnant patients who were hepatitis E positive has been enrolled in the study i.e. 1st January 2015 to 31st December 2017. Patients with chronic liver disease or hepatic failure due to other reasons were excluded from this study.

Data including vital characteristics of pregnant ladies (including age, parity, gestational period), maternal and foetal effects has been gathered from review of patient's admission file of the unit. These patients were treated according to the organization protocol. All pregnant ladies with fulminant hepatic failure be treated with supportive care in the intensive care unit in collaboration of the department of gastroenterology and Hepatology.

In this descriptive study percentages were calculated for qualitative variables like cause of fulminant hepatic failure, complications, maternal and foetal outcome. Mean Standard deviation were considered for age, duration of jaundice at admission, and laboratory investigations. SPSS version 18 was used for all statistical analysis. As this study was retrospective done on patients file, so ethical approval not necessary.

Socioeconomic Status

It was based on month to month salary.

- low socioeconomic group (month to month pay Rs. 4000-20,000/month)
- Middle class month to month pay >Rs. 20,000-100,000/month).
- Upper class (month to month pay >Rs.100,000-/month).[9]

Maternal Education

Maternal education was divided into five classes depending on the level of education (Illiterate, Primary, Middle, High, and Undergraduate

Residence

These are arbitrary definitions.

Urban

An Urban region was a focal city and encompassing zones whose population was greater than 50,000.

Rural

The rural area was defined as population below than 2,500 residents.

RESULTS

A total 168 patients with hepatitis –E associated fulminant hepatic failure in pregnancy were admitted at Isra University Hospital between 1st January 2015 to 31st December 2017. The mean age of the patients was 26.04±6.40 years (range 18 years to 47 years). Majority of the patients 123 (73.2%) had not received antenatal care (Table-I). Overall maternal mortality was 51 (30.3%) Table-II. Out of 168, 27 (16%) presented in the first trimester, 45 (26.7%) presented in the second trimester, while 96 (57.1%) patients developed fulminant hepatic failure in their 3rd trimester of pregnancy (Table-III). Out of 168, 111(66%) patients delivered and 57 (33.9%) were undelivered. Fetal and perinatal outcome of delivered patients showed miscarriage 45 (40.5%), stillborn 25(14.8%), preterm delivery 17(10.1%), neonatal death 7 (6.3%) and 17 (10.1%) new born remained alive.

Age (in years)	
Mean	26.04±6.40
Range	18-47
Residence	
Urban	57(33.9%)
Semi Urban	33(19.6%)
Rural	78(46.4 %)
Socioeconomic Status	
Lower	89(57.7%)
Middle	47(23%)
Upper	32(19.4%)
Maternal Education	
Illiterate	79(47%)
Primary	34(20.2%)
Middle	37(22%)
High	15(8.9%)
Undergraduate	2(1.1%)
Postgraduate	1(0.59%)
Antenatal Visits	
Booked	28(16.6%)
Unbooked	140(83.3%)

Table-I. Demographic data of study participants. (n = 168)

Variables:	Mean ± SD	Range
Age (years)	26.40 ±6.4	18-47
period of Jaundice at admission (days)	6.57±2.932	(3-15)
Improved n: (%)	117	(69.6%)
Died (%)	51	(30.3%)
Investigations		
Serum bilirubin (mg/dL)	21.144 ±6.722	(7.19-31)
SGPT (U/L)	609.50 ±305.4	(215-2550)
SGOT(U/L)	521.15 ±110.0	(274-962)
Serum Albumin (g/dL)	2.5962 ±.748	(1.50-3.50)
Prothrombin time	46.588 ±14.01	(33-74)
Blood sugar (mg/dL)	111.17 ±11.73	(45-120)
Complications n: (%)		
Encephalopathy	37	(22.0%)
DIC	21	(12.5%)
Renal failure	19	(11.30%)
Septicemia	17	(10.1%)
Ascities	9	(5.3%)
Cerebral Odema	9	(5.3%)
None	35	(20.8%)

Table-II. Clinical & laboratory parameters of pregnant women with hepatitis –E associated fulminant hepatic failure (n = 168).

Variables	Frequency (%)
Maternal outcome: Ist trimester (n=27)	
• Recover	23(13.6%)
• died	4(2.3%)
2nd trimester (n=45)	
• Recover	34(20.2%)
• died	11(6.5%)
3rd trimester (n=96)	
• Recover	60(35.7%)
• died	36(21.4%)
Delivered	111(66%)
Undelivered	57(33.9%)
Mode of delivery(111)	
Normal vaginal delivery	60(54%)
LSCS	6(5.4%)
Others	45(40.5%)
Fetal outcome (n=111):	
Miscarriage	45(40.5%)
Preterm delivery	17(10.1%)
Still born	25(14.8%)
Early neonatal death	7(6.3%)
Remained alive	17. (10.1%)

Table-III. Maternal & Fetal outcome with hepatitis –E associated fulminant hepatic failure in pregnancy (n = 168).

DISCUSSION

Our study on acute viral Hepatitis E associated with fulminant hepatic failure in pregnant ladies recognized that it is of great worry and has very serious cost.

Novel proof from epidemiological and clinical studies suggests that rate, morbidity and death from hepatitis E is very high in pregnancy, in our study the maternal mortality is 51(30.3%) while Shukla et al concluded 33.3% maternal mortality rate in patients with hepatitis E in pregnancy.[10]

In addition in utero transmission of HEV might happen often in moms with hepatitis E, and give to grave perinatal health outcomes.[11] In our previous study on etiology, clinical features and outcome of fulminant hepatic failure in pregnancy, HEV infection (53.8%) was the most common cause for liver failure with a mortality of 13.4%.[12] Saeed et al suggested much better prognosis in HEV patients than in other causes with severe liver failure.[13] While Lettau LA reported The HEV infection rates

in pregnant women from 17 to 40%.[14] Aggarwal R concluded HEV infection in 50-70% of all patients with periodic viral hepatitis in India.[15] While in another study the prevalence of HEV infection in third trimester was between 40-57%.[16] In our study mean age of the patients were 26.04±6.40, K Rajesh et all reported 46.7% of patients were under 25 years of age and were primigravida (57.7%).[17] Mishra et al also observed that majority (60%) of the hepatitis E infection among Indian pregnant women in below 25 years of age.[18] In present study highest infection has been found 96 (57.1%) in third trimester. Hepatitis E virus has been identified to transmit a disease to pregnant women but mortality rates as far above the ground as 20–25% has been observed in third trimester.[19] Commonest mode of delivery was normal vaginal delivery 60(54%) in our study, KRajesh et al also reported same findings.[17] In our study the major complications of FHF were encephalopathy 37 (22%) while Khuroo M.S observed cerebral edema (53.2%). Disseminated intravascular coagulation was similar in two studies.[20] The foetal out come in our study was miscarriages 45 (40.5%) preterm deliveries, 17 (10.1%) still born, 25 (14.8%) early neonatal deaths and 7 (6.3%) babies remained alive17(10.1%) Banait et al in Mumbai observed 29(69%) fetal deaths and 23(54%) maternal deaths in HEV in pregnant women which is very high in comparison to our results.[21]

"A variety of complex immunologic and hormonal changes throughout pregnancy impair cellular immunity by triggering adapter protein (ORF3 of HEV), which might enhance viral multiplication and lead to liberate of cytokines and liver cell death resulting substantially elevated morbidity and mortality".[22,23] HEV infection occurs as a result of transmission via oral route through unhygienic water and food. An enhancement in sanitary circumstances, accessibility of clean drinking water, appropriate sewage disposal, public education and wakefulness regarding clean defecation practice, proper washing of hands , use if sanitizers are the foundation for the prevention of hepatitis E.[1,24]

Basic awareness regarding the killing of hepatitis E viruses by boiling water at 100 °C or by proper chlorination can be extremely successful.[1,24]

CONCLUSION

- Hepatitis – E related fulminant hepatic failure in pregnancy is a troublesome clinical issue and connected with exceptionally high maternal and fetal mortality.

- Appropriate diagnosis, early timely intervention can considerably diminish the morbidity and mortality associated with (HEV) Fulminant hepatic failure.

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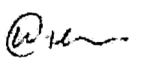
AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Zahida Parveen Brohi	Principal investigator, Conceptualization and design of the research work, data collection, literature search, statistical analysis and interpretation, drafting revision and writing of manuscript.	
2	Uzma Parveen	Data collection, drafting, revision and final approval.	
3	Aneela Sadaf	Statistical analysis, drafting, revision and final approval.