

*Full Length Research Paper*

# Effect of viral hepatitis on maternal and fetal outcome

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The outcome of Hepatitis during pregnancy has been observed to be broadly diverse by various researchers, ranging from the benign to fatal. A poor result has progressively been seen in pregnant women suffering Hepatitis in Pakistan. This study was planned to study the frequency, causative organisms and chief prognostic elements affecting the consequence of viral hepatitis in pregnant women. Sixty-eight pregnant ladies answering to the doctor's facilities with jaundice were enlisted and enrolled as cases and their hematological, biochemical and viral profiles were pondered. Sixteen non-pregnant women were chosen as controls and a comparable workup was carried out. A relationship was done between the two groups. We further separated the cases into two groups – survivors and non- survivors and attempted to discover the components anticipating mortality. The unpaired understudy t test and chi square test were utilized to figure out whether the distinctions were measurably noteworthy. All the information was entered and investigated utilizing SPSS form 20.0. Viral Hepatitis in pregnancy caused a very high maternal mortality (19.1%) and foetal wastage (42.6%). Hepatitis E virus was the commonest causative organism (77.9%) responsible for viral hepatitis during pregnancy. It also caused the highest maternal mortality due to fulminant hepatic failure. Maternal mortality was significantly higher in those women presenting with features of encephalopathy, SIRS, highbilirubin levels and prolonged prothrombin time. Vertical transmission was noted in Hepatitis B and E. Hepatitis E is the chief causative organism causing fulminant hepatic failure in pregnant women. It leads to very high rates of maternal mortality and foetal wastage.

**Keywords:** Viral Hepatitis, maternal outcome, fetal outcome.

## INTRODUCTION

Viral Hepatitis in pregnancy has incited a lot of debate and discussion throughout the world. Various authors [1,2] have reported findings ranging from no difference in foetal/maternal outcome to nearly universal fatality. Interestingly, these different types of outcome are peculiar to certain geographical areas. For example, there was no increased maternal mortality due to Hepatitis E infection in pregnancy in the reports from South India [3] and Egypt, [4] but a significantly higher rate

of mortality has been reported from North India.[5] This is despite the fact that all these geographical areas are endemic for Hepatitis E infection.[6]

Each type of Viral Hepatitis has its own concerns. Hepatitis A is a common cause of hepatitis transmitted by the faeco–oral route and does not influence the course of pregnancy. Hepatitis B, when acquired at or near delivery, is transmitted vertically in as high as 60% of unborn children. This has grave consequences for the child as nearly 90% of these infections shall become chronic and translate into Liver cirrhosis, Portal hypertension or Hepatocellular Carcinoma in the child. Hepatitis C is well known to get transmitted vertically and

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the virus may lead to Hepatocellular Carcinoma in the mother as well as the child. Hepatitis E, while remaining a self-limited, usually benign, hepatic infection in men and non-pregnant women, acquires a grave form in pregnant women. It shows an increased attack rate in pregnancy. The incidence of Fulminant Hepatic Failure and mortality rate is much higher than that associated with other hepatic viral infections. [1,6,7] Recently, the concern of vertical transmission of Hepatitis E has also been highlighted by various authors.[8] A review of the available literature showed that there is a wide variation in the clinical course and outcome of sporadic viral hepatitis in pregnancy.[9,10] No detailed study has been undertaken in Pakistan regarding this problem. Hence, this study was undertaken to find out the causes, clinical course and factors predictive of mortality in a cohort of pregnant women suffering from viral hepatitis.

## MATERIAL AND METHODS

All pregnant women with hepatitis reporting to the Department of Gynaecology and Obstetrics, Liaquat University Hospital, Hyderabad during the period of May 2012 to July 2014 were enrolled consecutively and prospectively in the study. This hospital is a tertiary care Centre, catering to a thickly populated area situated in Hyderabad, Sindh. The total number of cases studied was 68. The course of their pregnancy was closely followed and the end point of observation was the natural /artificial termination of pregnancy or death of the woman. The detailed Biochemical, Hematological and Virological workup was done for the women and the neonates who survived. The cases were compared with 16 controls who were non pregnant women with hepatitis. The number of surviving neonates who could be studied was ten. The biochemical workup included Liver function and Kidney function tests. Haematology included the blood picture, prothrombin time and INR. The virological studies included Anti- Hepatitis A IgM (for recent Hep A), Hepatitis B Surface Ag (for Hep B), Anti Hepatitis C IgM and IgG (for Hep C), Anti Hepatitis EIgM (for Hep E). Patients were evaluated for Hepatitis D only if Hepatitis B was found positive. Hepatitis Bcore antigen was tested when necessary. All women underwent Ultrasound of the abdomen. A comparison was done between the cases and controls regarding the type of viral hepatitis, biochemical and haematological picture and mortality.

Similarly, comparison was done between the 'survivor' and 'non survivor' cases regarding the type of viral hepatitis, biochemical and haematological picture. This was done to find out the factors responsible for maternal mortality. Unpaired Student t test, Chi square test were used to compare the results. A difference of < 0.05 was considered statistically significant.

## RESULTS

Most of the cases were young and in the age group of 21 to 25 years. The cases and controls were well matched

with respect to age. The predominant presenting symptom was jaundice.

The mean hemoglobin level of the cases as well as the controls group was low ( $7.87 \pm 2.36$  and  $8.13 \pm 2.28$  respectively) but the difference was not statistically significant,  $p=0.698$ .

The mean Total Leukocyte Count was much higher in the cases compared to the controls and this difference was statistically significant, ( $P=0.028$ ). This finding, along with the clinical features of tachycardia, fever etc. indicated a higher incidence of Systemic Inflammatory Response Syndrome (SIRS). No particular focus of infection was found and blood cultures could not be done due to technical reasons (patients had already received antibiotics pre-admission).

The average serum bilirubin, liver enzymes, serum proteins, prothrombin time, blood urea and creatinine levels were not significantly different on comparison of the cases and controls (Table 1).

The incidence of Hepatitis E was 77.9% in pregnant women and 25% in controls (Table 2). This difference was highly significant ( $p<0.001$ ). This could indicate a predilection of the Hepatitis E virus for pregnant women. No virus could be detected in 9 cases (13.2%) and 8 controls (50%). This difference was statistically significant ( $p=0.003$ ). This finding suggested a higher incidence of cryptogenic hepatitis among non-pregnant women.

The analysis of mortality rates revealed a very high maternal mortality rate of 19.1% in the cases. The rate of total foetal wastage was also found to be very high: 42.6% (Table 3).

We divided the cases into two further groups 'survivors' and 'non-survivors', comparing the clinical and laboratory findings between them. This was done to find out the various factors responsible for maternal mortality. Amongst the various biochemical parameters, the average Serum Bilirubin was found to be significantly higher among the non survivors ( $16.08 \pm 6.12$ ) as compared to the survivors ( $11.57 \pm 5.11$ );  $p = 0.0076$ . The average INR value was also found to be significantly higher in the 'non-survivor' group ( $2.40 \pm 2.00$ ) as against the 'survivor' group ( $1.12 \pm 1.0$ );  $p=0.0023$ .

Among the survivors, there were 41 women in 2nd trimester and 14 in 3rd trimester of pregnancy. Among the non-survivors, there were 7 in 2nd trimester and 6 in 3rd trimester. The trimester of pregnancy was not a significant factor for prediction of mortality.

Presence of encephalopathy at the time of admission correlated very closely with maternal mortality. All women who subsequently died (non-survivor group) had presented in varying grades of hepatic encephalopathy. Hepatitis E virus was the most common cause of Hepatitis among both 'survivors' and 'non-survivors' but there was no statistically significant difference in the rate of Hepatitis E infection between these two groups. The viral profile of the neonate could be studied only in 10 cases as most of these women were lost to follow up after delivery.

**Table 1.** Comparison of Blood parameters in two groups.

	<b>Cases</b>	<b>Controls</b>	<b>P value</b>
Haemoglobin	7.87±2.36	8.13±2.28	0.698
Total leukocyte Count	38236.36±91142.21	12478.69±7203.43	0.028
S Bilirubin	8.52±6.11	6.38±4.39	0.191
SGOT	335.95±566.87	406.13±449.09	0.646
SGPT	453.29±591.09	575.85±594.17	0.459
SAP	324.72±285.59	290.02±165.49	0.630
Protein	9.72±11.08	7.19±1.00	0.503
SG ratio	1.13±1.73	0.88±0.31	0.663
PT	26.19±23.02	27.69±26.20	0.832
INR	3.03±4.95	2.31±2.30	0.614
Urea	55.81±43.60	31.69±21.60	0.240
S. Creatinine	1.45±2.16	1.24±1.45	0.838

Statistically significant

**Table 2.** Comparison of type of Hepatitis in controls and cases.

<b>Type of Viral hepatitis</b>	<b>Cases (n=68)</b>	<b>Controls (n=16)</b>	<b>P value</b>
HAV positive	0	1(6.3%)	0.190
HBV positive	5(7.4%)	3(18.8%)	0.173
HCV positive	1(1.5%)	1(6.3%)	0.347
HEV positive	53(77.9%)	4(25.0%)	<0.001**
No Virus detected	09 (13.23%)	08 (50%)	0.003
Co-infection of two or more viruses	0	0	0

\*Statistically significant; \*\*Statistically highly significant

**Table 3.** Maternal and foetal outcome.

<b>Maternal Outcome</b>	<b>Number of patients (n=68)</b>	<b>%</b>
Survived	55	80.89%
Died	13	19.11%
<b>Foetal outcome</b>	<b>Number of patients (n=68)</b>	<b>%</b>
Survived	39	57.39%
Foetal Wastage	29	42.61%

Vertical transmission of the viral infection was observed in 3 out of the 10 neonates, out of which 2 had Hepatitis E and 1 had Hepatitis B.

## DISCUSSION

Acute Viral Hepatitis is a major public health problem in the developing countries. Most of the cases of Hepatitis in Pakistan have been attributed to Hepatitis E, for

which it is an endemic zone.[11-13]This infection can spread in epidemics[14,15] or sporadically, especially during the warm and rainy weather seasons. The presentation of Hepatitis E during pregnancy may range from the asymptomatic to fatal in different endemic areas. A worse prognosis had been noted by various authors when Hepatitis E occurs during pregnancy.[16-19]

In our study, Hepatitis E was found to be the main causative organism responsible for Hepatitis in 77.9%

pregnant women. This figure was higher than that reported by other authors from India, except Khuroo et al., [20] who have reported the rate of HEV infection amongst pregnant women as 86% (Table 5). Studies done from North India have revealed widely varying rates of Hepatitis E infection ranging from 32% to 86%. [1]

The notable finding in our study was the high rate of maternal mortality (19.1%). The high mortality rate was comparable to most of the other studies conducted in North India, ranging from 12% to 64%. This finding is in variance from certain other studies done in other parts of the world, e.g. a study from Egypt [4] revealed a very high rate of Hepatitis E infection (84.3%), but there was not a single case of maternal mortality. The seroprevalence of Hepatitis E IgG antibody was found to be low (33.67%) in New Delhi by Begum et al., [21] probably leading to higher rates of clinical disease and maternal mortality.

There may be many host factors responsible for the worse presentations seen in some studies. In our study, most of the women were anaemic and under nourished, but there was statistically no significant difference in the haemoglobin values of survivors and non survivors. [22]

A very important reason for the high maternal mortality in the present study appeared to be the delay in seeking medical help. This is evidenced by the large number of women reporting in hepatic encephalopathy and highly elevated bilirubin levels. The average Bilirubin levels were significantly higher in the non survivors (11.57mg% in survivors and 16.08mg% in non survivors;  $p=0.0076$ ). The INR was also significantly higher in the non-survivors compared to the surviving group. This correlated well with the SOFA scoring system [23] for prediction of mortality

The presence of features of encephalopathy at presentation was highly predictive of subsequent mortality. All the women who presented with features of encephalopathy succumbed early. This probably reflects on the delay in hospitalization of the patient. This finding corroborates well with that of Banait et al., [24] who found higher mortality among those women reporting in a higher grade of encephalopathy.

A number of social misconceptions regarding jaundice are rampant amongst the rural population in Sindh. The use of witchcraft for treatment of jaundice is very common in the population studied. This was found to be a frequent cause of delay in the patient seeking medical help. In addition to witchcraft, there is also the prevalent use of herbal medications for the treatment of jaundice, which might actually worsen the jaundice.

In our study, the trimester of pregnancy was not a predictive factor for mortality. This is in contrast to the study by Banait et al., [24] who found that survival rates improved in those women who delivered as against those who did not (after excluding the women who presented in grade IV encephalopathy). This finding had led to the speculation that induction of labour might

possibly help in reduction of maternal mortality. However, this hypothesis has not been confirmed due to ethical reasons.

The rate of foetal wastage was found to be very high – 42.6%. This was similar to the findings of Banait et al., [24] who reported an overall foetal mortality of 69%.

Vertical transmission was noted in Hepatitis B and E. Out of the 10 babies studied, 2 were positive for Hepatitis E and one for Hepatitis B. The remaining 3 neonates tested negative for all Viral Hepatitis markers. The exact rate of vertical transmission could not be estimated as most of the surviving neonates were lost to follow-up. However, the rate of vertical transmission of Hepatitis E appears to be lower than that reported by Singh et al – 50%. [8]

There are some shortcomings in our study. The sample size was small: hence prevalence rate could not be calculated. There could be a selection bias as the study was carried out in a tertiary care centre, hence only the women in a very critical condition would be reporting here.

## CONCLUSION

Viral hepatitis during pregnancy is an important cause of maternal mortality and foetal wastage in Sindh Hyderabad. In this study we found that hepatitis E is the chief causative organism of hepatitis during pregnancy. It shows an increased predilection for pregnant women compared to non-pregnant women.

## Conflict of interest

None to declare

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