*Original Article*

# Pregnancy Outcome in Impaired Liver Function in Pre-eclampsia

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**Abstract**

*Pre-eclampsia induced liver disease is a disorder unique to pregnancy and is frequently seen in third trimester. Severe pre-eclampsia is defined by extreme elevation in systemic blood pressure and evidence of organ compromise. HELLP syndrome is a unique liver related disorder of pregnancy that was first described by Weinstein in1982 as a constellation of clinical and laboratory abnormalities in pregnant women in their third trimester. This disorder was termed HELLP syndrome with (H) for haemolysis, (EL) for elevated liver enzymes and (LP) for low platelet counts. This is a severe variant of pre-eclampsia. Objective of this study was to determine the alteration of liver function in preeclampsia and its correlation with the clinical severity as well as the perinatal outcome. This was a one-year prospective observational cross sectional study included 100 patients with pre-eclampsia. Severity of the pre-eclampsia clarified clinically. Pre-eclampsia patients having history of hepatitis, cirrhosis of liver, gallbladder diseases and other pre-existing medical disorders that altered liver function were excluded from this study. The mean age of the patients was 25.3+4.9 years ranging from 18 to 37 years. One third of the patients (33.3%) were in the age group 28 to 32 years. Out of 100 patients, 58% belongs to poor income group. Among the studied samples 17% had epigastric pain and discomfort, 13% had complaints of vomiting and 43% develop severe pre-eclampsia. Among the Patients with altered hepatic enzyme level, 8.33% had complaints of epigastric pain, 6.66% complains vomiting. Maximum patients (66.6%) with elevated liver enzyme had no major complications whereas 33.4% of patients developed major complications. Patients with severe pre-eclampsia have elevated liver enzyme whereas patients of mild symptoms had normal liver enzymes level. Cases with raised serum biochemical markers had strong association with complications of severe pre-eclampsia. Pregnancy outcome in severe pre-eclampsia with hepatic involvement is grievous. Graves sequlae of pre-eclampsia can be prevented and minimized by timely institutional intervention. Post-partum followup would help to find out other parameters of pregnancy outcome.*

**Keywords:** *HELLP syndrome, pre-eclampsia, inpaired liver function*

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## INTRODUCTION

Abnormal liver function tests occur in 10 to20% 0f pregnancy complicated by pre-eclampsia and are associated with poor maternal and fetal outcome.[1] Blood level of liver enzymes differ from non-pregnant level to pregnant level. AST, ALT, GTT and bilirubin levels do not change during uncomplicated pregnancy from 16 to 40 weeks of gestation and are the same as the non-pregnant values. A cross sectional study of 304 women concluded that AST, ALT, GGT each show a significant increase for a gestational age of six months, but it is not clear whether this is compared with early pregnancy or to the non-pregnant control group. None of these paper define their laboratory references ranges.[2] Some author assume that LFT are not altered by pregnancy and advice using the non-pregnant laboratory reference ranges. In the absence of altered hepatic blood flow physiological haemodilution alone may result in lower reference ranges for AST, ALT, GTT and bilirubin in pregnancy if correct statistical methods are used to construct them[3].During pregnancy there is no histological changes in liver cells, alkaline phosphatase levels, other liver function tests (serum level of bilirubin, AST, ALT, LDH) are unchanged. It has been shown that pregnant women complicated with pre-eclampsia, there is marked changes in liver both structural and functional.[4] Periportal hemorrhagic necrosis of the liver occurs due to thrombosis of the arterioles. The necrosis starts at the periphery of the lobule. There may be sub capsular hematoma. Hepatic

insufficiency seldom occurs because of the reserve capacity and regenerative ability of liver cells. Liver function tests are especially abnormal in women with HELLP syndrome, is an acronym for hemolysis(H), elevated liver enzymes (EL) and low platelet (LP) count (<100000/mm3). HELLP syndrome is manifested by nausea, vomiting, epigastric or right upper quadrant pain, along with biochemical and hematological changes. Parenchymal necrosis of the liver causes elevation in hepatic enzymes (AST and ALT >70IU/L), LDH >600IU/L. Eventually liver may rupture to cause sudden hypotension, due to hemoperitoneum. This is a fatal condition both for the mother as well as for the baby which warrants urgent intervention.[5-9]

## METHOD AND MATERIALS

This was a hospital based prospective observational study carried out 100 pregnant women had symptoms of pre-eclampsia admitted to inpatient department of Obstetrics and Gynecology, Rajshahi Medical College Hospital, Rajshahi from January to December 2010. After admission a thorough history was taken followed by relevant clinical examination and some base line investigations. Then patient of pre-eclampsia categorized as mild or severe. Patients having features of severe pre-eclampsia were included in this study. Number of cases were 100. The features of severe pre-eclampsia are 1) persistent rise of blood pressure more than 160/110 mm of Hg 2) protein excretion of more than 5gm per 24 hours' urine 3) oliguria 4) platelet count less than100000 percubic mm of blood 5) HELLP syndrome 6) Cerebral or visual disturbances 7) Persistent severe epigastric pain 8) Retinal hemorrhages 9) IUGR of the fetus 10) Pulmonary edema. Patients having HELLP syndrome and severe epigastric pain underwent details investigations for liver functions. For liver function e.g. SGPT, SGOT, LDH, fibrinogen level, prothrombin time and serum bilirubin level were detected. Serum total protein and albumin level are usually reduced in pre-eclampsia. So these two parameters for assessing liver function in pre-eclampsia were avoided in this study. Serum uric acid level is one of the single most important parameter to assess fetal wellbeing. In this study serum uric acid level is measured to detect fetal affection due to pre-eclampsia with impaired liver function. Patients were managed according to hospital protocol. Maternal and fetal conditions were followed up till discharge. All necessary information was collected from the responders as per pretested data collection sheet by face to face interview after taking prior informed consent from them. The data were processed by computer and statistical analysis were performed by using the SPSS version.

## RESULTS

The study population consisted of 100 cases diagnosed as severe pre-eclampsia. Age range of the patients were 18 to 37 years. Most of the patients of severe pre-eclampsia were between 18 to 32 years. Relevant data were expressed as tabulated forms and figures.

Table-I Showed that the mean age of the case group was 25.3±4.9 years ranging from 18 to 37 years.33% of the cases were in the age group of 26-29 years.

**Table-I: Age group distribution of studied patients (n=100)**

| Age in years | Case (N) | Percent (%) |
|---|---|---|
| 18-21 | 14 | 14 |
| 22-25 | 30 | 30 |
| 26-29 | 33 | 33 |
| 30-33 | 13 | 13 |
| 34-37 | 06 | 06 |
| Total | 100 | 100 |

Table-II Showed represented that 57% of cases complained most of the ominous features of severe pre-eclampsia.

**Table-II: Distribution of Complaints of the severe pre-eclampsia**

| Complaints | Frequency (N) | Percent (%) |
|---|---|---|
| Headache | 15 | 15.00 |
| Epigastric pain | 15 | 15.00 |
| Vomiting | 05 | 05.00 |
| IUGR | 08 | 08.00 |
| All the above complaints | 57 | 57.00 |
| Total | 100 | 100.00 |

Table-III Showed represents that 23.25% patients having raised serum bilirubin, 23.25% having elevated liver enzyme. Altered biochemical markers were detected in 43%.

**Table-III: Distribution of severe pre-eclamptic patients by bio-chemical markers and hematological findings**

| Markers | Frequency | Percent |
|---|---|---|
| S.Bilirubin(>2mg%) | 10 | 23.25 |
| SGPT ( >70 IU/L) | 10 | 23.25 |
| LDH (> 600 IU/L ) | 10 | 23.25 |
| Fibrinogen(<150mg/dl) | 03 | 06.97 |
| Platelet count(<100000/mm | 10 | 23.25 |

Table-IV showed that cases with raised serum biochemical markers had strong association with complications of severe pre-eclampsia (p>.001).

**Table-IV: Association of pregnancy complications with hepatic enzyme level of the patients**

| Bio-chemical markers | No. of patients with complications | P-value |
|---|---|---|
| S.Bilirubin>2mg%(n=10) | 04 | .01 |
| SGPT>70IU/L (n=10) | 05 | .01 |
| LDH>600IU/L (n=10) | 03 | .05 |
| Fibrinogen<150mg/dl(n=03) | 01 | .05 |
| Platelet count<100000/mm(n=10) | 02 | .01 |

**Table-V: Distribution of patients by pregnancy outcome (n=100)**

| Pregnancy outcome | Frequency | Percent |
|---|---|---|
| No complications | 65 | 65% |
| Fetal complications | 20 | 20% |
| Maternal complications | 10 | 10% |
| Both maternal & fetal complications | 05 | 05% |

Table-VI: Shows revealed that when serum uric acid level raised probability of fetal affection also raised (P =0.23).

**Table-VI: Fetal outcome related to serum uric acid level (n=100)**

| Serum uric acid level | Fetal affection | P value |
|---|---|---|
| <6mg%(n=75) | 02 | 0.02 |
| >6mg%(n=25) | 23 | 0.23 |

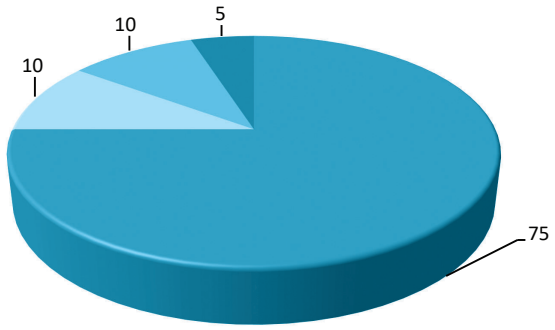


**Figure 1:** *Fetal outcome in pre-eclamptic patients of hepatic impairment*

- No Effect on fetus-75%
- IUGR-10%
- Perinatal Death-10%
- IUD-5%

## DISCUSSION

An estimated 50000 women per year worldwide die from pre-eclampsia.[10] Most women with pregnancy induced hypertensive disorders are symptomless, which is an important point for frequent antenatal visit particularly in late pregnancy. Laboratory test are used for prediction, diagnosis and monitoring of disease process. There is no test that reliably indicates who will develop this polymorphic disease.[11] The diagnosis of pre-eclampsia is based on the laboratory test. Treatment is restricted to symptomatic and expedited delivery is only the way to resolve the disease.[12] Severe pre-eclampsia usually develops in the late second or early third trimester and accompanied by significant proteinuria. Here we studied 100 patients with severe pre-eclampsia[13]. In this study incidence was found 6.3% of hospital admission. The study was done by Hossain in 1993 showed the incidence of pre-eclampsia was 7.6%.[14] The incidence was 7.1% in 2003,a study done by Khan.[15] The incidence of pre-eclampsia in hospital practice varies from 5-15%.[16] Young primigravid and elderly pregnant patients are vulnerable to develop pre-eclampsia and eclampsia. 33.3% of studied group of patients were from 26-30 years of age. It correlates with the study done by Das, a study of 100 cases at IPGMR in 1997.[17] The incidence of severe preeclampsia was 46.7%. Patients of this group were found elevated serum uric acid level and liver enzymes.[18] Serum uric acid seems to be a sensitive indicator of fetal wellbeing.[19] 66.6% of patients having elevated liver enzyme but severe pre-eclampsia had no complications. These group of patients were admitted at 37$^{th}$ completed

weeks.[20] Termination of pregnancy were done timely and judiciously. So, pregnancy outcome was satisfactory without fetal as well as maternal complications. Rest of the patients were developed complications like.[21]

1) Post-partum eclampsia
2) Heart failure
3) Acute kidney injury 4) Abruptio placentae
5) Pulmonary edema
6) IUGR
7) IUD

Serum bilirubin level is elevated more than 2 mg%in 23.25% and pregnancy outcome was very poor. When SGPT level raised pregnancy complicated 10%. The prevalence of elevated liver functions in pre-eclampsia in this study was higher than previously documented. This is not surprising as it is likely that abnormal liver function reflects vasoconstriction involving the hepatic bed and thus widespread disease.[22] It is also possible that some of the AST and GTT is not of hepatic origin, both are widely distributed throughout the body and may be elevated in relation to pre-eclampsia by haemolysis or endothelial injury respectively.[23] McMahon suggested that in HELLP syndrome early changes in liver function may be due to red cells destruction and that liver damage itself only occurs later.[24] Nonetheless this would not alter the outcome variables associated with abnormal liver function tests. Alternatively, the prevalence of abnormal liver function tests may be inflated by the use of multiple ranges which itself increases the probability of classifying as abnormal a woman is in fact normal.[25-28] We recommended that pregnancy specific reference ranges were used for the assessment of liver function in the antepartum period. This may be particularly useful in the management of pre-eclampsia, where underestimation of abnormal liver function will be avoided more accurate assessment of the severity of the disease possible.[29-32]

## CONCLUSIONS

Pre-eclampsia considered as high risk pregnancy. The correlation between the severity of pre-eclampsia and impairment of liver function indicates that mild or severe pre-eclampsia and eclampsia are manifestations of different maternal responses. An strong association was fund in raised serum biochemical markers due to impaired liver function and complication of severe pre-eclampsia. This study revealed that one third of the patients (33.33%) belonged to the young adult age group (21-30 years) one out third (33%) of patients with severe pre-eclampsia had hepatic involvement. Among the patients, 25% had fetal jeopardy but maternal death was not found. Most of the patient referred from remote area. Post-partum follow-up would help to find out other parameters of pregnancy outcome. Graves sequlae of the disease can be prevented and minimized by timely institutional intervention.

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