Original Article

A Study of Liver Function Tests among pregnant women with Pre-eclampsia

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ABSTRACT:

Pre-eclampsia is defined as the development of hypertension, proteinuria or both after 20 weeks, in a woman with previously normal blood pressure. Hepatic dysfunction with pre-eclampsia has long been recognised. It is a multisystem disorder that affects various systems of the body. Our present study was conducted on pregnant women as well as women with pre-eclampsia, attending the Antenatal Outdoor Patient Department of R. G Kar Medical College, Kolkata. The results showed an increase in Serum Aspartate Transaminase(AST), Alanine Transaminase(ALT) and Alkaline Phosphatase(ALP) levels in the pre-eclamptic women than those with normal pregnancy. Thus, it may be suggested that if the Liver Function Test results are found to be elevated, the patients should be taken care of immediately and appropriately, to arrest further progress of the disease.

Key Words: Pre-eclampsia, Pregnancy, Liver Function Tests.

Introduction:

During pregnancy, the energy requirement of the body is greatly increased. This is associated with high food consumption and increase in maternal body metabolism. Histological studies revealed that the changes were associated with both cellular hyperplasia and hypertrophy. [1] Disorders arising in pregnancy such as acute fatty liver of pregnancy, hemolysis, pre-eclampsia and eclampsia, elevated liver enzymes and low platelets [HELLP] syndrome, cholestasis, hyperemesis gravidarum and isolated cases of raised liver enzymes can impose serious problems. Abnormal liver function tests can occur in 20 % to 30% of pregnant women who develop pre-eclampsia. [2] Hepatic dysfunction with pre-eclampsia has long been recognized. [3] Pre-eclampsia is defined as the development of hypertension, proteinuria or both after 20 weeks, in a woman with previously normal blood pressure. [4] It is more common in women during their first pregnancy, women with obesity [5], diabetes [6] or who have gestational hypertension [4], [7] , [8] . It even occurs in pregnant women who develops new onset hypertension and proteinuria after 20 weeks of gestation. [9] Moreover, pre-eclampsia is a multisystem disorder, affecting the Central Nervous System, the liver, the kidney as well as the coagulation system. [10] Hence, they are associated with poor maternal and fetal outcomes. [11], [12] More recently, this dysfunction has been associated with other findings of HELLP

Syndrome that complicates the course of 3 -10% patients of pre-eclampsia. In India, the incidence of pre-eclampsia is about 7 -10% among all hospital based antenatal admissions. [13]

The presence of a placenta is necessary and sufficient to cause the disorder. Loganathan et al [14] in 2000-2001 undertook a study amongst 175 healthy pregnant South Indian women. The study showed lower albumin, lower AST (Aspartate Transaminase) & ALT (Alanine Transaminase) level & raised ALP (Alkaline Phosphatase) against their non-pregnant control. In yet another study conducted in Calicut Medical college in 2003-2005, the authors found most abnormal LFT (Liver Function Tests) results in 3rd trimester (59.2%). HELLP syndrome stood out to be one of the cause of abnormal LFT in 3rd trimester. [15] Girling et al reported a higher prevalence of elevated liver function tests in pre-eclamptic group (54%) than gestational hypertension. [16] Thus, changes in values of LFT occur during normal pregnancy, and understanding these physiological changes is needed for proper management of liver diseases. In the light of above facts, the present study was conducted in a tertiary referral hospital of Kolkata, depicting the results of LFT during normal pregnancy and women presenting with pre-eclampsia.

Materials & Methods:

The present study was conducted within a period of May 2005- April 2006 amongst pregnant mothers, who were attending the Antenatal Outdoor Patient Department of a tertiary level referral hospital, at R. G. Kar Medical College, Kolkata. The study population consisted of 150 Bengali Hindu women within the range of 22 – 30 yrs. 38 non-pregnant healthy women served as a control group, keeping the age group in the range. Amongst the rest, 30 women were in 1st trimester, 27 in 2nd trimester and 30 in 3rd. 25 women were suffering from pre-eclampsia. The disease was diagnosed on basis of hypertension (diastolic Blood Pressure more than 90 mm of Hg) and proteinuria. Informed consent was taken from all patients.

Liver Function tests (LFT) were performed in each trimester of normal pregnancy & pregnant women with pre-eclampsia. All the selected patients were normoglycemic. The LFTs included serum bilirubin (conjugated & unconjugated fraction), Aspartate transaminases (AST/ SGOT), Alanine transaminases (ALT/SGPT), Alkaline phosphatase (ALP), total protein with albumin- globulin ratio & prothrombin time. All the patients were primigravidae, normoglycemic & normotensive except in those of pre-eclampsia group. The patients had normal past medical & surgical history and general examinations were within normal limit. Detailed drug history assured the selection of patients who took only iron, folic acid & calcium as supplements. Patients taking any other drugs were excluded from the study. Patients having history of hepatic derangement in recent past & extreme

degree of malnutrition, infective hepatitis, biliary obstruction were also excluded. The patients of 2nd & 3rd trimester and pre-eclamptic patients had mild anemia induced by the condition itself. But none of them had any other concurrent illness. They had no significant medical & surgical history. Menstrual history was normal.

Estimation of serum bilirubin was done by reacting it with diazotized sulfanilic acid (Kit supplied by Merck India Ltd., Mumbai). Estimation of transaminases (AST & ALT) were done by kinetic method with the kit supplied by Pinnacle Marketing Pvt. Ltd., Mumbai. ALP was estimated by kinetic method with the help of kit supplied by the same company. Serum total protein was estimated by reacting with Biuret reagent using Kit by Pinnacle Marketing Pvt. Ltd. & Albumin by Bromocresol Green method using the reagents supplied by the same company. All the tests were done by Chem-pro model of Semiautoanalyser (Transasia). Prothrombin time was taken using the kit of Thrombospan 2S supplied by Span Diagnostic Ltd. (utilizing rabbit brain thromboplastin). USG was done in all pregnant patients & liver with gall bladder was evaluated.

Results:

Serum bilirubin was normal in all the three trimesters of pregnancy. But transaminases were more than control group. Serum ALP gradually increased in 2nd & 3rd trimesters. Rise of ALP in 3rd trimester pre-eclamptic patients was more than that of 3rd trimester of normal pregnancy. No significant alteration of serum albumin, globulin & Albumin: Globulin ratio was found during normal pregnancy and pre-eclampsia.

Table-1

Showing Liver Function Tests during 1st Trimester of Pregnancy in women:

Tests	***Control (Mean±S.D)***	***Pregnancy in 1st Trimester (Mean± S.D)***
Total Bilirubin(mg/dl)	0.7 ± 0.04 (38)	0.76 ± 0.06 (30)
Conjugated Bilirubin(mg/dl)	0.4 ± 0.04 (38)	0.46 ± 0.04 (30)
AST/SGOT(U/L)	33.1 ± 3.21 (38)	59.8 ± 6.92 (30)
ALT/SGPT(U/L)	32.14± 4.56 (38)	55.3 ± 6.82 (30)
Alkaline Phosphatase(U/L)	70.67 ± 7.22 (38)	161.5 ± 18.33 (30)
Total Protein(g/dl)	6.82 ± 0.26 (38)	7.18 ± 0.24 (30)
Albumin(g/dl)	3.93 ± 0.18 (38)	4.12 ± 0. 09 (30)
Globulin(g/dl)	2.9 ± 0.22 (38)	3.06 ± 0.2 (30)
Albumin: Globulin	1.38 ± 0.17 (38)	1.44 ± 0.1 (30)
Prothrombin time(Sec)	14±0.5(38)	14±0.43(30)

The number in parentheses is the number of observations.

Table-2

Showing Liver Function Tests during 2nd Trimester of Pregnancy in women:

Tests	***Control (Mean±S.D)***	***Pregnancy in 2nd Trimester (Mean±S.D)***
Total Bilirubin(mg/dl)	0.7± 0.04 (38)	0.66 ± 0.05 (27)
Conjugated Bilirubin(mg/dl)	0.4 ± 0.04 (38)	0.37± 0.03(27)
AST/SGOT(U/L)	33.1 ± 3.21(38)	47.33 ± 6.82(27)
SGPT(U/L)	32.14± 4.56(38)	48.42± 7.35 (27)
Alkaline Phosphatase(U/L)	70.67 ± 7.22 (38)	209.83 ± 25.93(27)
Total Protein(g/dl)	6.82 ± 0.26 (38)	7.49 ± 0.12(27)
Albumin(g/dl)	3.93± 0.18 (38)	3.85±0.78 (27)
Globulin(g/dl)	2.9 ± 0.22(38)	3.58± 0.14 (27)
Albumin: Globulin	1.38 ± 0.17 (38)	1.15 ± 0.04 (27)
Prothrombin time(Sec)	14± 0.5(38)	14.4±0.5(27)

The number in parentheses is the number of observations.

Table-3

Showing Liver Function Tests during 3rd Trimester of Pregnancy in women:

Tests	***Control*** ***(Mean± S.D)***	***Pregnancy in 3rdTrimester*** ***(Mean± S.D)***
Total Bilirubin(mg/dl)	0.7 ± 0.04 (38)	0.77 ± 0.05(30)
Conjugated Bilirubin(mg/dl)	0.4 ± 0.04 (38)	0.41 ± 0.04 (30)
AST/SGOT(U/L)	33.1 ± 3.21 (38)	60.3 ± 5.8(32)
ALT/SGPT(U/L)	32.14 ± 4.56 (38)	60.6 ± 5.18 (30)
Alkaline Phosphatase(U/L)	70.67 ± 7.22 (38)	306.2 ± 37.6 (30)
Total Protein(g/dl)	6.82 ± 0.26 (38)	6.94 ± 0.29 (30)
Albumin(g/dl)	3.93 ± 0.18 (38)	3.81 ± 0. 11 (30)
Globulin(g/dl)	2.9 ± 0.22 (38)	3.13 ± 0.3(30)
Albumin: Globulin	1.38 ± 0.17 (38)	1.35 ± 0.15(30)
Prothrombin time (Sec)	14 ± 0.5 (38)	14.6± 0.44 (30)

The number in parentheses is the number of observations.

Table-4

Showing Liver Function Tests in women with Pre-eclampsia :

Tests	***Pregnancy in 3rd Trimester (Mean± S.D)***	***Pregnancy in Pre-eclampsia (Mean± S.D)***
Total Bilirubin(mg/dl)	0.77 ± 0.05 (30)	0.67 ± 0.04 (25)
Conjugated Bilirubin(mg/dl)	0.41 ± 0.04 (30)	0.38 ± 0.03 (25)
AST/SGOT(U/L)	60.3 ± 5.8 (30)	288.9 ± 80.58 (25)
SGPT(U/L)	60.6 ± 5.18 (30)	278.7 ± 70.7 (25)
Alkaline Phosphatase(U/L)	306.2 ± 37.6 (30)	520.4 ± 76.39 (25)
Total Protein(g/dl)	6.94 ± 0.29 (30)	6.65 ± 0.28 (25)
Albumin(g/dl)	3.81 ± 0. 11 (30)	3.27 ± 0.22 (25)
Globulin(g/dl)	3.13 ± 0.3 (30)	3.38 ± 0.01 (25)
Albumin: Globulin	1.35 ± 0.15 (30)	0.97 ± 0.06 (25)

The number in parentheses is the number of observations.

Discussion:

Liver serves multiple functions, the bio-transformation of insoluble compounds (drugs, toxins, bilirubin), metabolism & excretion of cholesterol & bilirubin, synthesis of plasma protein & metabolism of carbohydrates, lipids & amino acids. As metabolism & synthetic function of liver increase in pregnancy, it may be seen to alter its function. But in practice it may not always take place. Mild to moderate rise in LFT is associated with drug induced hepatotoxicity, hyperemesis gravidarum, cholelithiasis, HELLP Syndrome & acute fatty liver in pregnancy [17]. Bacq et al observed slightly higher ALT activity in 2nd trimester in normal pregnancy [18].

ALP is a marker that is normally used to identify cholestasis. The term serum ALP is applied to a group of enzymes that catalyze hydrolysis of phosphate esters at an alkaline Ph. These enzymes are widely distributed and may originate from bone,

liver, intestine, kidney and placenta. The significant rise of ALP activity during normal pregnancy in this study is in agreement with Riely (1994) [19], Samuels and Cohen (1992) [20], Smoleniec and James [21] and Sjogren [22]. These authors reported three to fourfold elevation of ALP levels in normal pregnancies, secondary to placental ALP levels. ALP activity may be elevated due to cholestasis and biliary obstruction; however, it is unlikely due to cholestasis in this study as bilirubin levels were normal in all the pregnant women.

The enzymes whose elevation in serum reflects damage to hepatocytes are markers of hepatocellular injury. These are AST and ALT. Elevation of ALT & AST during pregnancy is frequently associated with viral hepatitis. They catalyze transfer of alpha amino group of aspartate and alanine to the alpha-keto group of alpha amino group of alpha-keto gluteric acid. AST is found in the liver, cardiac and skeletal muscle in decreasing order of concentration. ALT is found primarily in the liver. Moderately elevated aminotransferase level (3-20fold rise) is typical of acute and chronic hepatitis. Any type of liver cell injury can cause moderate elevation in the serum aminotransferase. Level up to 300 unit/L are non-specific and may be found in any type of liver disorder. The present study did not show any change in these enzyme activities during normal pregnancy, rather an increase in its activity in third trimester of pre-eclampsia was observed. This is agreement with Riely [19] and Samuels and Cohen [20] . Sibai et al (1993) [23] reported that liver dysfunction is a feature of pre-eclampsia detectable by elvation of circulating hepatic enzymes, that may progress to jaundice and severe hepatic impairment[24] (Davies et al, 1980).

Sibai et al [23] reported that liver dysfunction is a feature of pre-eclampsia, detectable by elevated circulating liver enzymes, which may progress to jaundice and severe hepatic impairment [24]. Typical symptoms include epigastric pain and vomiting, but they are not always present [25] (Sheehan and Lynch, 1973). Macroscopically, the liver shows diffuse petechial hemorrhage over Glissson's capsules. Histopathological features are hepato-cellular necrosis with hemorrhages in periportal regions and deposition of fibrin without any inflammatory infiltrate. Thrombi can be detected in capillaries in the portal tract and occasionally in branches of hepatic arteries and portal vein [26] (Rolfe and Ishak, 1986). A vascular theory is now favoured. Segmental vasospasm results in injury to the endothelial cells and exposure to sub-endothelial collagen leading to platelet adherence, aggregation and precipitation of fibrin[26] . However, in our present work no histopathological study was undertaken. But, it may be suggested that if transaminase activity is found to be elevated, the patients should be taken care of immediately and appropriately to arrest

further progress of the disease. The present study was conducted with pregnant mothers attending in R.G.Kar Medical College, Kolkata. It shows no significant change in serum bilirubin, serum transaminases, serum protein & prothrombin time as compared to the control group. Table-1, table-2 and table-3 shows LFT in control vs pregnancy. They show that total serum bilirubin, conjugated bilirubin, serum AST & ALT level is increased in 2nd trimester of pregnancy as compared to other trimesters. Serum ALP starts rising at the 2nd trimester due to presence of placental isoenzyme. At the 3rd trimester this is more accentuated due to the placental fraction as well as hepatic fraction of ALP because at this stage there is centrilobular bile stasis [27]. Table-4 shows the increase in serum AST, ALT & ALP in pre-eclampsia of pregnancy which in accordance with the findings of Barron. [3] So, it can be concluded from the present study that the excretory, metabolic & synthetic function of liver (as evidenced by serum bilirubin, serum transaminases & serum protein level respectively) are surprisingly normal in normal pregnancy in spite of the increased metabolic burden.

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