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# Liver function tests in first and third trimesters of normal pregnancy in a population of North Kerala

**Sonia Venugopal,[1] Rajamma C K [2]**

**Abstract:**

**The aim of the study was to compare the first and third trimester variations of liver function tests during normal pregnancy in the age group of 20 to 30 years. It was a comparative prospective study wherein 100 pregnant women attending out-patient department for routine antenatal check-up were included. History was taken and general physical examination, systemic examination, routine investigations and liver functions tests were performed. Liver function tests were performed by an autoanalyzer. Analysis was done using student's t-test. P-value less than 0.05 was taken as significant. The serum total bilirubin, direct bilirubin, indirect bilirubin, aspartate amino transferase, total protein, albumin, globulin and gamma glutamyl transferase levels were higher in the first trimester when compared to the third trimester. The serum alanine amino transferase and alkaline phosphatase levels were higher in the third trimester when compared to the first trimester. There was not much significant difference between the A/G ratio and serum prothrombin levels in first trimester compared to that of third trimester. The decrease in total bilirubin, direct bilirubin, indirect bilirubin, total proteins, albumin and globulin were due to a phenomenon called hemo-dilution. The decrease in gamma glutamyl transferase could be due to the effect of hormones, oestrogen and progesterone which increases during pregnancy. Alkaline phosphatase levels increase by third trimester due to placental synthesis. Prothrombin time does not show any change in both the trimesters which shows that pregnancy has no effect on prothrombin time.**

**Keywords: Liver function tests, pregnancy, physiological variation, hemodilution**

## Introduction:

Pregnancy results in profound changes in maternal physiology in metabolism. These changes which are tolerated well in the normal gravid women can cause deleterious effects in those with pre-existing problems.[1]

During pregnancy, the serum oestrogen & progesterone levels increase progressively and reach a maximum during third trimester.[2] These sex steroids have effects on metabolic, synthetic and excretory hepatic functions.[3] Pregnancy may be associated with mild cholestasis owing to higher concentrations of oestrogen. Severe liver disease leading to acute liver failure is a complication of pregnancy. Major adaptation in maternal anatomy, physiology and metabolism is required for successful pregnancy.[4]

The aim of the study was to evaluate the changes in serum levels of routine liver function tests i.e., Alkaline phosphatase (ALP), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Gamma glutamyl transferase (GGT), direct and indirect bilirubin, total proteins, Albumin, Globulin, A/G ratio, prothrombin time (PT) during first & third trimesters in North Kerala.

## Materials & Methods:

This was a prospective study conducted in 100 pregnant women who attended the obstetrics and gynaecology (OBG) out-patient department (OPD) of Kannur Medical College, Anjarakandy for routine antenatal check-up.

The inclusion criteria were the patients in

age group 20-30 years with no history of medical complications. They were followed up in their first & third trimesters of pregnancy. Patients with hypertension, diabetes, liver diseases and those on drugs like non-steroidal anti-inflammatory drugs (NSAIDs), anti-epileptics, anti-tubercular drugs, drugs for thyroid disorders and oral contraceptives were excluded from the study.

Approval of the Institutional Ethics Committee was obtained and informed consent taken from all subjects. History, general examination, systemic examination & routine obstetric examination were done in all subjects. Blood samples were collected from all subjects during first & third trimesters. Serum bilirubin, AST, ALT, alkaline phosphatase, serum protein and PT were measured using fully random access clinical chemistry analyser Humastar-300. In the study, the liver function tests which were measured in 100 pregnant women who were not on any medication prior to pregnancy.

Descriptive and inferential statistical analysis using Student's t-test was carried out and significance assessed at 5% level of significance. The data was analysed using statistical software SPSS 16.0.[5-9]

## Results:

This was a hospital-based prospective study to find any variations in liver function tests during first and third trimester.

The serum total bilirubin levels were higher in the first trimester when compared to the third trimester which was statistically significant. The serum direct bilirubin levels were higher in the first trimester when compared to the third trimester and the P-value was statistically significant. The serum indirect bilirubin levels were higher in the first trimester when compared to the third trimester and was statistically significant. The serum aspartate aminotransferase levels were higher in the first trimester when compared to the third trimester and was statistically significant. The serum alanine aminotransferase levels were higher in the third trimester when compared to the first trimester and the P-value was statistically significant.

The serum total protein levels were higher in the first trimester when compared to the third trimester and the P-value was statistically significant. The serum albumin levels were higher in the first trimester when compared to the third trimester. The serum globulin levels were higher in the first trimester when compared to the third trimester. There is not much significant difference between the A/G ratio in first trimester compared to that of third trimester and the P-value was 0.296 which was statistically insignificant. The serum gamma glutamyl transferase levels were higher in the first trimester when compared to the third trimester, whereas serum alkaline phosphatase levels were higher in the third trimester when compared to the first trimester and the P-value was statistically significant. The serum prothrombin levels were similar in the first and the third trimester and P-value was not statistically significant.

## Discussion:

During pregnancy, the human body undergoes several changes in the process of its adaptation to the growing fetus. Although, these changes are physiological, there is potential for morbidity and mortality to both mother and fetus. Liver is the site of many important metabolic and synthetic functions of the body. Every pregnancy is a stress to the body. It affects every organ system and there are physiological changes in all the organs. Abnormal liver function tests occur in 3% to 5% of pregnancies, with many potential causes including co-incidental liver disease and underlying chronic liver disease. Several physiologic changes occur during pregnancy and could pose

**Table I: Statistical data of liver function tests in normal pregnancy**

| Test | Group | Mean | SD | t | P-value |
|---|---|---|---|---|---|
| Total Bilirubin | I trimester | 0.6840 | 0.08130 | 10.722 | 0.000 |
| | III trimester | 0.5640 | 0.06439 | | |
| Direct Bilirubin | I trimester | 0.2560 | 0.0675 | 9.470 | 0.000 |
| | III trimester | 0.1780 | 0.04837 | | |
| Indirect Bilirubin | I trimester | 0.4270 | 0.05478 | 5.029 | 0.000 |
| | III trimester | 0.3810 | 0.06919 | | |
| Aspartate Aminotransferase | I trimester | 22.51 | 3.07317 | -11.688 | 0.000 |
| | III trimester | 26.68 | 2.98102 | | |
| Alanine Aminotransferase | I trimester | 28.09 | 2.97157 | -8.648 | 0.000 |
| | III trimester | 32.55 | 2.55989 | | |
| Total protein | I trimester | 7.185 | 0.21195 | 19.342 | 0.000 |
| | III trimester | 6.617 | 0.14978 | | |
| Albumin | I trimester | 3.7030 | 0.14457 | 11.585 | 0.000 |
| | III trimester | 3.43 | 0.13446 | | |
| Globulin | I trimester | 3.482 | 0.16229 | 13.886 | 0.000 |
| | III trimester | 3.194 | 0.16740 | | |
| A/G ratio | I trimester | 1.0678 | 0.07546 | -1.05 | 0.296 |
| | III trimester | 1.0815 | 0.10741 | | |
| Gamma Glutamyl Transferase | I trimester | 18.33 | 2.14172 | 15.313 | 0.000 |
| | III trimester | 13.46 | 1.62319 | | |
| Alkaline phosphatase | I trimester | 67.02 | 10.94244 | -48.780 | 0.000 |
| | III trimester | 2.5115 | 35.43336 | | |
| Prothrombin time | I trimester | 13.12 | 0.327 | 0.217 | 0.829 |
| | III trimester | 13.11 | 0.314 | | |

difficulty in evaluating hepato-biliary function because they may be misinterpreted as pathological.

A study by Bacq et al was done in 103 healthy pregnant women and in 103 age matched controls not receiving oral contraception. They also found that total and free bilirubin concentrations are decreased during all three trimesters of pregnancy, as was conjugated bilirubin during the second and third trimesters.[10] Alkaline phosphatase activity was significantly higher in the third trimester. Serum aspartate aminotransaminase activity did not have any change between pregnant and non-pregnant women. Serum alanine aminotransferase activity was slightly higher in the second trimester

pregnant women than in controls. Serum gamma glutamyl transferase activity was significantly lower in the second and third trimesters.

However, in our study, serum total bilirubin, serum direct bilirubin and indirect bilirubin levels showed a decrease in levels in the blood from first trimester to third trimester. Hemodilution could at least be partly responsible for the decrease in bilirubin concentration because albumin is the protein that transports bilirubin.

In another study by Mitra AK et al on liver disorders during pregnancy and their management, bilirubin levels remain in the normal range. If raised, it tends to be conjugated hyperbilirubinemia.[11]

In another study by Gohel et al, serum total and direct bilirubin concentrations were significantly lower in second and third trimester. Serum ALT and AST activity was slightly but significantly increased in third trimester. Serum ALP activity was significantly higher in second and third trimesters. ALP activity increases as pregnancy advances. Serum GGT values were significantly lower in third trimester. No significant change was seen in serum total proteins concentration but serum albumin concentration was significantly lower and serum globulin concentration was significantly higher in all three trimesters. Serum albumin/globulin ratio was significantly reduced in second and third trimesters[12].

In this study, we found that the ALT activity was significantly higher during the third trimester than in first trimester. This result was similar in two other studies. However in the study by Maryam, the serum AST in activity was during all semesters not significantly higher than the control group. Bacq et al also found no change in ALT activity. In this study, we found significant increase in AST levels in the third trimester. Though there was a statistically significant decrease in serum AST, these are physiological normal values of AST in both the trimesters of pregnancy. However, study by Bacq et al had an increase in AST in the second trimester of pregnancy. AST levels in first and third trimesters remained the same.

A study by Elliot et al concluded that the serum ALT and AST values were higher in the pregnant women than the non-pregnant[13]. A study by Knopp et al was done to analyze the effects of pregnancy and oral contraceptive use on plasma glucose concentrations, hepatic, renal and thyroid function tests. Serum ALT and AST values were significantly high in pregnancy. They correlated this result by concluding that some serum glutamic oxaloacetic transaminase comes from the placenta.[14]

It was found in our study that the alkaline phosphatase levels showed a very large increase from first trimester to third trimester. Study by Bacq et al also had the same result.

In the study by Wakim- Fleming J et al, they found that high serum alkaline phosphatase levels are usually signs of benign changes in the liver during pregnancy.[15]

A study by Valenzuela et al revealed that

1. Placental ALP activity in serum is increased during pregnancy (from a value of zero in the non-pregnant woman) then disappears from the circulation.
2. Bone ALP activity is increased during pregnancy, and remains so, six weeks post-partum, in non-lactating women.
3. Total and placental, but not bone, ALP activities were lower at delivery, in women with premature rupture of membranes and those in pre-term labor than in normal-term controls.[16]

In the study by Elliot et al, the ALP analysis was done to see if the increase in serum alkaline phosphatase activity observed in pregnant woman could be of placental origin. It was found that alkaline phosphatase activity increases during pregnancy and that the increase is primarily in placental Alkaline Phosphatase that is heat stable.[13]

By contrast, serum alkaline phosphatase levels have been found to be lower in oral contraceptive users. This increase during pregnancy is not due to an increase in hepatic isoenzyme but rather largely due to the production of the placental isoenzyme.[17]

Our study showed that serum protein levels are found to decrease from first to third trimester. Even albumin and globulin levels are found to decrease from first to third trimester. Serum albumin levels decrease during the first trimester and this decrease becomes accentuated as the pregnancy advances.[10] The decrease in serum concentration is explained by the hemodilution phenomenon. Indeed, the intravascular mass of albumin has been found to be normal in pregnancy compared to controls. The increase in plasma volume that occurs during pregnancy led to hemodilution and decreased the protein concentration.

In the present study, gamma glutamyl transferase levels are found to slightly decrease from the first trimester to the third trimester of pregnancy. In the study by Bacq et al, there was a slight but significant difference in GGT in second and third trimesters in pregnant women. It was suggested that hepatic synthesis of GGT could be inhibited by hormone secretion during pregnancy. A significant decrease in serum GGT activity was also found in late pregnancy compared with early pregnancy in women with morning sickness.[18]

Our study showed that on change in prothrombin time from first trimester to third trimester of normal pregnancy, there was no significant change between the two trimesters.

In a study by Olorunshola et al, the result of PT showed no statistically significant difference in the first and third trimesters except in the second trimester. Hence it was concluded that pregnancy is not likely to have any adverse effect on prothrombin time.[19]

A study by Cerneca et al also recorded no change in the mean prothrombin time values among pregnant women but there was a statistically significant difference in second trimester when compared with the control group.[20]

A study by Uchikova et al studied the changes in haemostatic variables during normal pregnancy and compared them with the corresponding variables in a control group of non-pregnant women and found that pregnant women had statistically significant higher values for prothrombin time. The conclusion was that there is activation of coagulation during pregnancy, but it is counter balanced by activation of fibrinolysis, which maintains haemostatic balance.[21]

## Conclusions:

Physiologic changes that occur in every organ system during pregnancy cause alteration in normal laboratory values associated with hepatic function. Important markers of liver disease remain within normal limits including bilirubin, alanine aminotransferase, aspartate aminotransferase, gamma glutamyl transferase and prothrombin time. The serum bilirubin levels which included the direct and indirect bilirubin, were comparatively decreased in the third trimester. Serum proteins which were albumin and globulin also showed a mild but statistically significant decrease in the third trimester. GGT levels also showed a decrease across the two trimesters due to hemodilution. The serum AST and ALT levels showed a mild increase in the third trimester but remained below physiological normal limits. The only drastic increase found was in the value of alkaline phosphatase. Alkaline phosphatase is a poor means of diagnosing cholestasis during pregnancy. Prothrombin time did not change from the first to the third trimester, It meant that pregnancy did not have any influence on prothrombin time. The elevation in aminotransferases or

gamma glutamyl transferase in pregnancy above physiological limit should trigger a search for disease.

Knowing the likely causes of an abnormal liver function test in the various stages of pregnancy helps allay much anxiety and allows appropriate obstetric planning with regards to the timing of delivery.

So, a thorough knowledge of physiological and pathological variations in different organ systems can help guide the pregnant woman through her gestational period without ending in a catastrophe.

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**Authors details:**

1- Post-graduate student, Department of Physiology, Kannur Medical College, Anjarakandy, Kannur, Kerala

2- **Corresponding author:** Associate Professor, Department of Obstetrics and Gynaecology, Kannur Medical College, Anjarakandy, Kannur- 670612, Kerala, India; **E-mail**: sushritan@gmail.com