

STUDY OF LIVER FUNCTION PARAMETERS IN PREGNANT WOMEN ATTENDING A TERTIARY CARE CENTRE

Biochemistry

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ABSTRACT

Introduction: Changes in liver biochemical profile are normal during pregnancy. However, severe liver disease, although rare, can occur and must be recognized at an early stage to reduce morbidity and mortality for mother and infant. The pathological derangement in the liver functions may be related to pregnancy or may coexist with pregnancy and may be divided into three major groups. We aim to find the incidence and possible (pregnancy-specific liver disorder and pregnancy non-specific liver disorder) of alteration in liver function tests (LFTs) in pregnant women attending tertiary care center.

Aim and Objectives: To determine the association between altered Liver function tests and Possible causes of liver disorders in Pregnancy.

Materials and Methods: Sampling data was collected over a period time of 1 Year. The study was done at the Clinical Biochemistry Department, tertiary care rural center. All data will be collected from the solace-laboratory Information system of the clinical biochemistry register at the central diagnostic laboratory. The sample size of the study is 83. Then, we plot the data according to the incidence of variable causes of liver disorder-specific and non-specific to pregnancy, also calculate the degree of alteration in LFTs in particular causes.

Result: This study included a total of 83 individual cases (females only-age 18 to 35 years). 41 (49%) out of 83 cases were related to pre-eclampsia, 12 (14%) cases related to HELLP syndrome, 2 (2%) cases related to AFLP, 3 (4%) cases related to ICP, 7 (8%) cases related to viral hepatitis, 3 (4%) cases related to Hyperemesis, 8 (10%) cases related to Eclampsia & 7 (8%) cases related to Miscellaneous. ALP level increase in viral hepatitis (mean 585.4 u/L, SD± 68.5), pre-eclampsia (mean 239.28 U/L, SD ± 38.25) and decrease level in miscellaneous Causes (mean 82.2 u/L, SD± 37.4) & ICP (mean 103.3 u/L, SD±30.0).

The AST level was rise in viral hepatitis (mean 781.8 µ/L, SD ± 46.14), AFLP (mean 708.5 u/L, SD ± 12.0), ICP (mean 100 u/L, SD ± 4.35), pre-eclampsia (mean 123.3 u/L, SD ± 22.0) and remain normal in miscellaneous cause (mean 21.2 u/L, SD ± 8.22) & hyper emesis (mean 25.66 u/L, SD ± 4.50).

Conclusion: Alterations in Liver function test results were due to Liver disease in pregnancy include -a 3-to-4-fold rise in the level of alkaline phosphatase (ALP) in viral hepatitis, Pre-eclampsia & AFLP. An increase in the total bilirubin level was found in viral hepatitis, pre-eclampsia & HELLP syndrome, whereas a downward trend was seen in the levels of serum albumin and total proteins. Serum ALT & AST levels become a rise in Pre-eclampsia, Viral hepatitis, Eclampsia, and also AFLP. It was found that serum AST level was in normal limits in hyperemesis & miscellaneous.

KEYWORDS

Pre-eclampsia, HELLP syndrome, AFLP (acute fatty liver of pregnancy), ICP (intrahepatic cholestasis of pregnancy), viral hepatitis, hyperemesis, Liver function test.

INTRODUCTION:

The liver is our body's most important organ after the heart, performing many important functions including metabolism, detoxification, and formation of important compounds including blood clotting factors and albumin¹. Liver disease has steadily gained recognition as a major health problem. Liver function parameters are Bilirubin, Total protein (TP), alkaline phosphate (ALP), Globulin (GLB), Albumin (ALB), Alanine Transaminase (ALT), Aspartate Transaminase (AST), and Lactate Dehydrogenase (LDH).

Pregnancy induces profound changes in the mother, resulting in significant alterations in normal physiology. Some of these changes influence normal biochemical values while others may mimic symptoms of medical disease. It is important to differentiate between normal physiological changes and disease pathology².

The underlying disorder can have a significant effect on the outcome of both mother and fetus, and diagnostic workup must be initiated urgently. The physiological changes in a pregnant woman can confuse the clinical by some nonspecific symptoms such as nausea, vomiting, and abdominal pain². Although these changes are physiological, there is potential for morbidity and mortality to both mother and fetus³. Pregnancy results in profound changes in lateral physiology in metabolism. During pregnancy, the serum estrogen and progesterone level increase progressively and reach a maximum during the third trimester⁴.

Alterations of laboratory test results representing the physiological changes of pregnancy include a threefold to fourfold increase in the level of alkaline phosphatase and also an increase in the synthesis of clotting factors, whereas a decrease in the levels of anti-thrombin 3 and protein serum albumin and total proteins⁵. Preeclampsia may further be

complicated by the involvement of the liver and kidney to different extents. Because although the plasma albumin level remains to decrease throughout the normal pregnancy. Serum Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels remain within the normal limits⁶. An increase in extracellular fluid volume during pregnancy leads to abnormal liver functions. Serum albumin, AST, ALT and total bilirubin decrease in normal pregnancy while ALP increases because it is also produced by the placenta⁷.

Changes in liver biochemical profile are normal during pregnancy. However, severe liver disease, although rare, can occur and must be recognized at an early stage to reduce morbidity and mortality for mother and infant⁸. The pathological derangement in the liver functions may be related to pregnancy or may coexist with pregnancy and may be divided into three major groups. The first group includes liver disorders that are specific to pregnancy such as hyperemesis gravidarum, pre-eclampsia, eclampsia, syndrome of hemolysis, elevated liver test and low platelets (HELLP), acute fatty liver of pregnancy, and intrahepatic cholestasis of pregnancy. The second group including occurs during the progress of another liver disease like viral hepatitis and herpes simplex. Third groups include pregnancy with pre-existing liver diseases such as chronic active hepatitis, cirrhosis of the liver, portal hypertension, and hepatic tumor. The guidelines for pregnancy-related liver disorders are not very clear in India and abroad⁹. We aim to find the incidence and possible (pregnancy-specific liver disorder and pregnancy non-specific liver disorder) of alteration in liver function tests (LFTs) in pregnant women attending tertiary care center.

MATERIALS AND METHODS:

The study was done at the Clinical Biochemistry Department, tertiary

care rural center of Gujarat. All Data (Liver functions tests, History, Diagnosis,) will be collected from the Solace-laboratory Information system of the clinical biochemistry register at the central diagnostic laboratory. No additional tests and no other investigation were carried out.

Data was to be taken retrospectively (1 year) and prospectively (1 year) from the Solace-Laboratory information system of Obstetrics wards resister and antenatal OPD resister. The sample size of the study is 83. After obtaining participants' details like history (obstetrics, past, drug), diagnosis, and Liver Function tests data, we plot the data according to the incidence of variable causes of liver disorder-specific and non-specific to pregnancy, also calculate the degree of alteration in LFTs in particular causes.

Inclusion Criteria:

Include all pregnant women attending antenatal OPD and admitted in our obstetric unit of the hospital with age 18 to 35 years during the study period.

Exclusion Criteria:

Women with chronic liver disease, Alcoholic individuals, Liver failure, Drug induce abnormal liver function test Samples required for this study were collected from the pregnant individuals who visited a tertiary care rural center. Blood (4-5 ml) was collected in a plain tube. Samples are then sent to the Central Diagnostic Laboratory of Shree Krishna Hospital. Samples are centrifuged for 20 min at 3000 rpm. Sample which is hemolyzed, lipemic, insufficient quantity, or without complete labeling of patient information, are rejected. After centrifugation samples were processed in the Biochemistry laboratory for the testing of Bilirubin, Total protein, ALP, ALB, GLB, ALT, AST & LDH. The tests were performed on Dimension RXL MAX & Dimensions XPAND PLUS.

A detailed history was taken from LIS – Laboratory Information System with the consent of CEO, Health Check Scheme in charge & Head of the Central Diagnosis Laboratory – CDL. Ethical Clearance was taken with the Institutional ethical committee with no. IEC/HMPCMCE/105/Faculty/10/21/19. We have performed Descriptive data analysis for statistical analysis.

Before starting the analysis, the instrument was calibrated using calibrators and the controls were checked at different concentrations of the analytes. As a part of external quality assurance, our laboratory is enrolled in Bio-Rad-USA external quality control programmers.

RESULT:

This study aims to determine - associations between altered LFTs and possible causes of liver disorders in pregnancy (pregnancy-specific & Pregnancy Non-specific).

Table: 1 Age-wise distribution table

Age	Number	Percentage
18-23	25	30%
24-29	39	47%
30-35	19	23%
total	83	100%

This study included a total of 83 individual cases. It included females only (age 18 to 35 years). In our study (Percentage-wise), From total percentages, there were 30 % in between 25 cases (18-23 age), 47 % in between 39 cases (24-29 age) & 23 % in between 19 cases (30-35 age) pregnancy women present.

Table: 2 Total number and percentages of individual causes.

Causes	number	percentage
Pre-eclampsia	41	49%
HELLP syndrome	12	14%
AFLP (acute Fatty Liver of pregnancy)	2	2%
ICP (intrahepatic cholestasis of pregnancy)	3	4%
Viral hepatitis	7	8%
Hyper emesis	3	4
Eclampsia	8	10
Miscellaneous	7	8
TOTAL	83	100

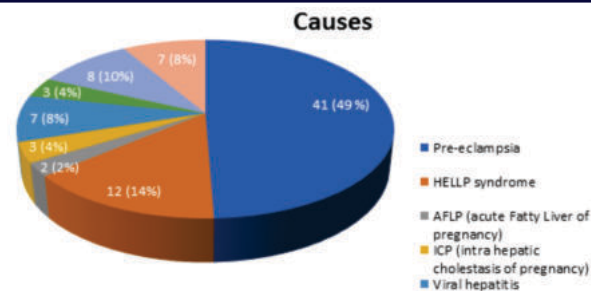


Figure: 1 Total number and percentages of individual causes.

In the present study, there were several numbers of causes, such as Pre-eclampsia, HELLP syndrome, AFLP (acute fatty liver of pregnancy), ICP (intrahepatic cholestasis of pregnancy), viral hepatitis, hyperemesis, Eclampsia & Miscellaneous. As above pie diagram, 41 (49%) out of 83 cases were related to pre-eclampsia, 12 (14%) cases related to HELLP syndrome, 2 (2%) cases related to AFLP, 3 (4%) cases related to ICP, 7 (8%) cases related to viral hepatitis, 3 (4%) cases related to Hyperemesis, 8 (10%) cases related to Eclampsia & 7 (8%) cases related to Miscellaneous.

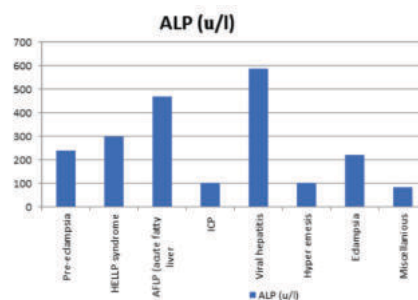


Figure: 2 Serum ALP results according to causes.

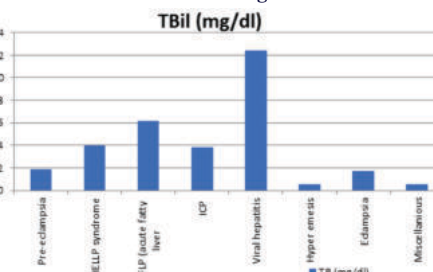


Figure: 3 Serum TBIL results according to causes

From the discussion of the above graph of parameters performed in the present study, ALP level increase in viral hepatitis (mean 585.4 u/l, SD $\pm$ 68.5), pre-eclampsia (mean 239.28 U/L, SD $\pm$ 38.25), and decrease level in miscellaneous Causes (mean 82.2 u/l, SD $\pm$ 37.4) & ICP (mean 103.3 u/l, SD $\pm$ 30.0).

The total bilirubin level was found raise in viral hepatitis (mean 12.45 mg/dl, SD $\pm$ 1.13), pre-eclampsia (mean 1.85 mg/dl, SD $\pm$ 0.90 mg/dl) and low level in hyper emesis (mean 0.57 mg/dl, SD $\pm$ 0.12), miscellaneous causes (mean 0.58 mg/dl, SD $\pm$ 0.29) and others causes level variable.

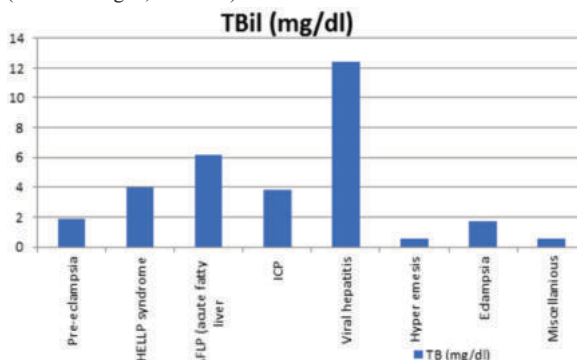


Figure: 4 Serum DBIL results according to causes

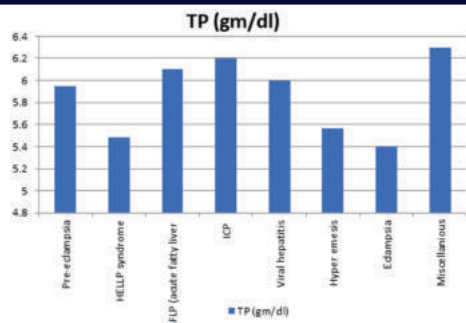


Figure 5 Serum TP results according to causes

As per above diagram, direct bilirubin grading was rise in viral hepatitis (mean 11.26 mg/dl, SD $\pm$ 1.44), AFLP (mean 5.95 mg/dl, SD $\pm$ 0.07) and lowest level in hyper-emesis (mean 0.236 mg/dl, SD $\pm$ 0.08) and miscellaneous causes (0.192 mg/dl, SD $\pm$ 0.08).

The total protein was decrease in miscellaneous causes (mean 6.3 mg/dl, SD $\pm$ 1.25), ICP (mean 6.2 mg/dl, SD $\pm$ 1.24), AFLP (mean 6.1 mg/dl, SD $\pm$ 0.5656) and level lower in eclampsia (mean 5.40 mg/dl, SD $\pm$ 0.69) & HELLP syndrome (mean 5.48 mg/dl, SD $\pm$ 1.06).

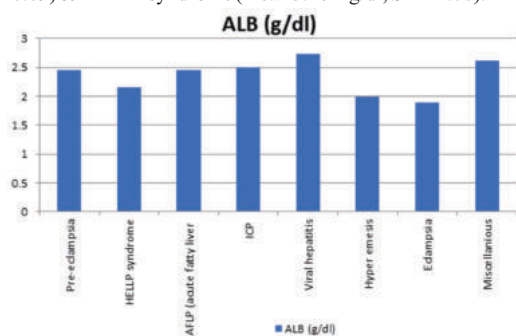


Figure 6 Serum Albumin results according to causes

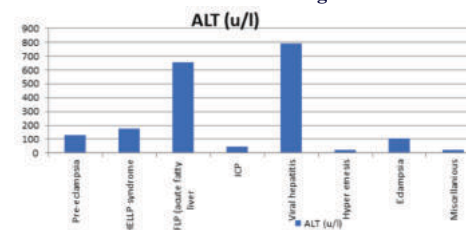


Figure 7 Serum ALT results according to causes

Diagram no:7 & 8, ALB Level is slight lower than normal range in most of all causes like viral hepatitis (mean 2.72 g/dl, SD $\pm$ 0.52), miscellaneous causes (mean 2.62 g/dl, SD $\pm$ 0.99), and more decrease in eclampsia (mean 1.9 g/dl, SD $\pm$ 0.35) & hyper emesis (mean 2.0 g/dl, SD $\pm$ 0.45).

As per the above chart, ALT is higher than the normal in viral hepatitis (mean 792.85 u/l, SD $\pm$ 79.61), AFLP (mean 655.0 u/l, SD $\pm$ 7.07), and decrease level in miscellaneous causes (mean 20.8 u/l, SD $\pm$ 4.26), hyperemesis (mean 21.0 u/l, SD $\pm$ 0.72) & ICP (men 49.33 u/l, SD $\pm$ 52.88).

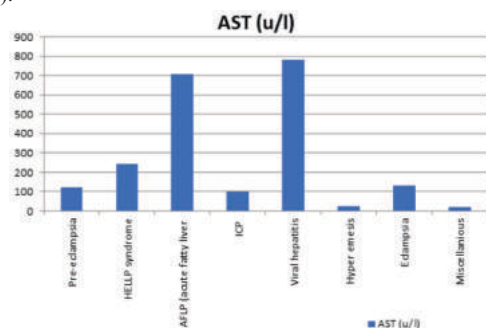


Figure 8 Serum AST results according to causes

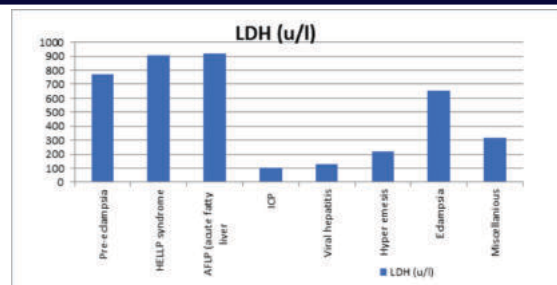


Figure 9 Serum LDH results according to causes

As per the above column graphs, the AST level was a rise in viral hepatitis (mean 781.8 u/l, SD $\pm$ 46.14), AFLP (mean 708.5 u/l, SD $\pm$ 12.0), ICP (mean 100 u/l, SD $\pm$ 4.35), pre-eclampsia (mean 123.3 u/l, SD $\pm$ 22.0) and remain normal in the miscellaneous cause (mean 21.2 u/l, SD $\pm$ 8.22) & hyperemesis (mean 25.66 u/l, SD $\pm$ 4.50).

The LDH level is very high than that of the normal range as per the above chart in AFLP (mean 919.0 u/l, SD $\pm$ 63.63), HELLP syndrome (mean 906.8 u/l, SD $\pm$ 108.7), pre-eclampsia causes (mean 771.3 u/l, SD $\pm$ 111.8) and normal grade in ICP (mean 104.6 u/l, SD $\pm$ 6.50), viral hepatitis (mean 132.0 u/l, SD $\pm$ 24.49), hyperemesis (mean 219.3 u/l, SD $\pm$ 22.85).

DISCUSSION:

Liver diseases during pregnancy are a challenging situation for both the fetus and the mother. Pregnant women of a younger age are more likely to have abnormal LFT. In most studies, the cause of abnormal LFT is reported to be pregnancy-specific disorder and varies from 60% to 80%^{9,10}. The mean ALT, AST, and ALP levels showed increased values in viral hepatitis and AFLP. Sumangali et al. compared liver function and they also reported an increased ALT, AST, and ALP level in viral hepatitis and AFLP⁵.

In this study, serum albumin level was decreased as the pregnancy advanced, and the same result was marked by the study of Maryam et al. The increase in plasma volume that occurs during pregnancy led to hemodilution and decreased the serum protein concentration¹.

The mean of LDH was very high in pre-eclamptic, AFLP & HELLP women as Dang et al. also found that LDH is less specific than AST and ALT as a marker of hepatocyte injury. However, it is markedly elevated after an ischemic liver injury¹¹.

Overall, observing all parameters from data related to liver disease, we conclude that the most of parameters are a rise in viral hepatitis and AFLP (acute fatty liver of pregnancy).

CONCLUSION:

In our present study, Alterations in Liver function test results were due to Liver disease in pregnancy include - a threefold to fourfold rise in the level of alkaline phosphatase (ALP) in viral hepatitis, Pre-eclampsia & AFLP. An increase in the total bilirubin level was found in viral hepatitis, pre-eclampsia & HELLP syndrome, whereas a downward trend was seen in the levels of serum albumin and total proteins. Serum ALT & AST levels become a rise in Pre-eclampsia, Viral hepatitis, Eclampsia, and also AFLP. It was found that serum AST level was in normal limits in hyperemesis & miscellaneous.

The limitations of the present study were that being a hospital data-based study, though we had taken a large sample size, it was still advisable to conduct similar studies with more participants with specific trimester of pregnancy and in diverse geographical areas. More participants would help in establishing a better study of liver function parameters in pregnant women attending a tertiary care hospital.

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