Evaluation of Liver Function Tests in Normal Pregnancy-An Observational Epidemiological Study-Kumbakonam Urban Rural Epidemiological Study-KURES 10

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Abstract: Early interpretation of liver function tests (LFTs) can result in timely management and it may decrease the incidence of complications in both the mother and the foetus. Normal LFTs don’t always imply a normal liver. A number of drawbacks can occur when interpreting basic blood LFTs. Abnormal Liver Function Tests (LFTs) in pregnancy must be properly interpreted to avoid diagnostic pitfalls. we did a routine testing in 498 asymptomatic antenatal mothers in the third trimester. Ninety-seven percentagge of mothers had normal bilirubin while 93 % had normal enzyme levels. The other abnormal values were also within 1 to 1.5 % above the normal. No mother had any symptoms. Only two patients had gallstones whose LFTs were normal. Two mothers had tattoo marks while the other two were HbsAg positive. All the 498 mothers had an uneventful progress towards delivery. Cross consultation done on a few cases with abnormal values were non-contributory. Pregnancy-related disorders are the most common reason for unusual liver function tests during pregnancy, especially in the third trimester. We omitted such cases to support our hypotheses of avoiding undue testing. The most prevalent is pre-eclampsia-related disorder. This is the first such study on a huge sample size. We suggest a routine testing of LFTs is not needed in otherwise healthy antenatal mothers.

Keywords: Pregnancy, liver, laboratory, test and Epidemiological
INTRODUCTION

Pregnancy doesn’t really modify the liver size, but the growing uterus displaces the liver superiorly and posteriorly in the third trimester, so a palpable liver indicates significant hepatomegaly and implicit liver problems. The physiological changes in liver function that occur during pregnancy are usually transient and very seldom permanent. Pre-eclampsia and eclampsia, acute fatty liver of pregnancy (AFLP), hemolysis, increased liver enzyme, and reduced platelets (HELLP) syndrome, cholestasis, hyperemesis gravidarum, and isolated cases of elevated liver enzymes can all have serious consequences. Pathological abnormalities in liver functions can be related to or may coexist with pregnancy, and they can be classified into three major groups. The first category includes pregnancy-specific liver disorders such as hyperemesis gravidarum, pre-eclampsia, gestational hypertension, the HELLP syndrome of hemolysis, elevated liver test and low platelets, acute fatty liver of pregnancy, as well as intrahepatic cholestasis. These conditions are mostly trimester-specific. Intercurrent liver disease that occurs during pregnancy, such as viral hepatitis and herpes simplex, is included in the second group. Pregnancy with pre-existing liver disease, such as chronic active hepatitis, falls into the third category. Early interpretation of liver function tests (LFTs) can lead to timely management, potentially reducing complications in both the mother and the foetus. Normal LFTs do not necessarily indicate a healthy liver. When analysing basic blood LFTs, a number of pitfalls can occur. LFTs are frequently used to evaluate liver injury rather than liver function. Disordered LFTs can imply that something is wrong with the hepatic function and provide clues to the nature of the problem, but this is seldom the case. Changes in the biochemical profile of the liver are normal during pregnancy. In an otherwise asymptomatic mother, routine ordering of LFTs is becoming the norm. Any minor change necessitates additional testing and consultation. It’s critical to distinguish between normal physiological changes and disease pathology. The major hypotheses question in our study was that a routine liver function testing is not needed in otherwise healthy parturients. As a result, we decided to perform the following LFTs on asymptomatic pregnant women and possibly question the need for a routine testing.

METHODS

2.1 Study Participants

This prospective observational study was carried out with the necessary ethical approval and patient consent. (IRBSTH/104/2021- 11/04/2021). The research was carried out in accordance with the Helsinki Declaration. The selected patients were from an obstetric hospital near Puducherry, India who were willing to take part in the study. An informed consent was taken from all of them.

2.2 Selection Criteria

The inclusion criteria were asymptomatic pregnant mothers with willingness to undergo the tests. The exclusion criteria were any systemic illness. Any recent viral infections like Dengue, recent or current liver disease or any congenital abnormality to change the test profile. The parturients with known drugs which deranges the liver function are also excluded.

2.3 Study Protocol

The variables noted were the patient’s age, gravida, gestational age, occupation, type of diet, any known liver illness and severe symptoms, hypertension, diabetes, tattooing, and hepatotoxic drugs. The investigations were conducted between 26 and 28 weeks of pregnancy by accredited and validated equipment.

2.4 Liver Function Analyses

A survey scan of the mothers’ abdomen for the liver and gallbladder was performed.

1. Bilirubin, both direct and indirect
2. Proteins in serum
3. alkaline phosphatase, SGOT, and SGPT
4. Prothrombin time will be measured if there is a significant derangement.

We intended to collect 500 continuous simple convenient samples from willing patients. Only asymptomatic patients were accepted, whereas mothers with symptoms were not.

2.5 The Abnormal Patients and Physical Examination

The mothers whose values were abnormal had specialist opinion and suggested follow up with no other treatment. As all patients were asymptomatic, they did not undergo any further testing. All asymptomatic HbsAg positive mothers were followed by the specialist.

3. STATISTICAL ANALYSIS

A simple continuous sampling willing mothers were selected. The data collected were entered in an excel sheet and subjected to simple descriptive analyses using SPSS software (USA) 21 version and the results displayed. The study is about a simple descriptive analysis of normal and abnormal liver function tests in abnormal patients. As such a complicated data analyses is not part of our protocol.
4. **RESULTS**

The results are tabled below (Table 1).

<table>
<thead>
<tr>
<th>S.No</th>
<th>Parameter</th>
<th>Values in Mean(SD) or n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age</td>
<td>27.12 (4.23)</td>
</tr>
<tr>
<td>2</td>
<td>Hemoglobin</td>
<td>10.85 (1.51)</td>
</tr>
<tr>
<td>3</td>
<td>Bilirubin (normal)</td>
<td>483 (97)</td>
</tr>
<tr>
<td>4</td>
<td>Elevated bilirubin (&gt;1.1)</td>
<td>15 (3)</td>
</tr>
<tr>
<td>5</td>
<td>Reduced STP (&lt;5.5 mg/dl)</td>
<td>19 (3.8)</td>
</tr>
<tr>
<td>6</td>
<td>STP (5.5 mg/dl)</td>
<td>479 (96.2)</td>
</tr>
<tr>
<td>7</td>
<td>Normal transaminase levels</td>
<td>429 (86.1)</td>
</tr>
<tr>
<td>8</td>
<td>Elevated transaminase levels (&gt;32 U/L)</td>
<td>69 (13.9)</td>
</tr>
<tr>
<td>9</td>
<td>Normal ALP</td>
<td>459 (92.2)</td>
</tr>
<tr>
<td>10</td>
<td>Elevated ALP (&gt;229 U/L)</td>
<td>39 (7.8)</td>
</tr>
<tr>
<td>11</td>
<td>Hb &gt;10 g/dl</td>
<td>377 (75.7)</td>
</tr>
<tr>
<td>12</td>
<td>Hb &lt;10 g/dl</td>
<td>121 (24.3)</td>
</tr>
</tbody>
</table>

Using 1.1 mg as the cut off value for serum bilirubin, 97 percent of antenatal mothers had normal levels. Only 3% had abnormal values, but they were all less than 1.5 mg percent. Alkaline phosphatase levels were normal in approximately 92 percent of mothers. The mothers were all asymptomatic. Two were found to be HbSAg positive with normal laboratory values. Tattooing was done in two cases, and gallstones were discovered in two more antenatal mothers. All these above six patients had normal blood tests.

5. **DISCUSSION**

Serum ALP and albumin levels decrease with gestational age, while ALT levels rise\(^2\). All whilst, AST, GGT, and bilirubin levels fluctuate but remain within non-pregnant women’s normal ranges. Unless these normal, gestation-related alterations are considered when evaluating LFT values in a pregnant woman, physiologic adaptations of pregnancy may be misinterpreted as pathologic, or pathologic findings may be missed\(^3\). In our study, more than 90% have normal values and...
the remaining had minimal elevations to be significant in terms of clinical disease. Guarino et al. have found the abnormal tests to be 3 – 5 % of pregnancies which go along with our findings.

Pradumna et al. have found the elicitation of abnormal tests during pregnancy led to unnecessary consultant visits. Even though there are a few studies in this topic, with less sample size, this is the first such study on a huge sample size. Innumerable screening tests have already been in vogue during the antenatal period. One study found that pre-eclamptic antenatal women had higher serum uric acid, ALT, and AST levels than normotensive counterparts, and the variations were statistically significant. As a result, serum uric acid and liver function tests may be used to detect pre-eclampsia-related end-organ damage and be considered as biomarkers. Hence the idea of taking the liver function tests as a routine should not be popularised. Terrault have suggested to vigilantly look for dysfunction in antenatal mothers if they have clinical liver dysfunction.

Intrahepatic cholestasis of pregnancy (ICP) is a pregnancy-specific liver disease. It is distinguished by pruritus and increased serum bile acids and/or aminotransferase levels. ICP usually appears during the third or second trimester of pregnancy and continues to improve on its own after delivery. We did have a few rare cases of gall stones but there were no clinical features of ICP in these cases. Pregnant women experience physiological changes that really can imitate liver disease; thus, they must be taken into account in the diagnosis of women with presumed liver disease. We did not encounter any specific or non-specific liver disease in our big sample size. Variations in liver function tests during a normal pregnancy can be misconstrued as pathological, masking or exacerbating preexisting disease. Thus, identifying and comprehending these physiological changes during pregnancy is critical for the detection of liver diseases in pregnancy. They have studied the differences in LFT in various trimester which we have not done. When compared to nonpregnant women, that very many values of liver function tests are still below the normal upper limits during normal pregnancy. Any increase in serum ALT and AST activity levels, as well as serum bilirubin, should be considered pathologic and should be investigated further. Khatun et al. have also described a reduction in the values during pregnancy and caution should be exercised in the interpretation of results. There are no clearcut guidelines of doing LFTs in the antenatal period.

6. CONCLUSION

Ninety-seven percentage of mothers had normal bilirubin while 93 % had normal enzyme levels. All are asymptomatic. We conclude that such routine testing is not needed in asymptomatic patients with no other illness like preeclampsia.

7. AUTHOR CONTRIBUTION

MRS – concept and design, TSS – data collection, SPS – manuscript writing and supervision

8. CONFLICT OF INTEREST

Conflict of interest declared none.