

## **Frequency and Etiology of Altered Liver Function in Pregnancy**

**Hira Najam, Fahmida Parveen Memon, Shumaila Naeem, Afsheen Memon**

**Dr. Hira Najam**

FCPS Part-II Trainee

Liaquat University of Medical & Health Sciences  
(LUMHS), Jamshoro, Sindh-Pakistan.

**Dr. Fahmida Parveen Memon** (*Corresponding Author*)

Assistant Professor

LUMHS, Jamshoro, Sindh-Pakistan.

Email: dr\_memon16@yahoo.com

**Dr. Shumaila Naeem**

Post Graduate MS (OBGY) Trainee

LUMHS, Jamshoro, Sindh-Pakistan.

**Dr. Afsheen Memon**

Post Graduate Trainee

LUMHS, Jamshoro, Sindh-Pakistan.

**ABSTRACT**

**OBJECTIVE:** To determine the frequency of etiology of altered liver function in pregnancy in patients admitted to a tertiary care hospital.

**METHODOLOGY:** This was a Descriptive Cross-sectional study conducted at the department of obstetrics and gynecology Liaquat University of Medical and Health Sciences Hyderabad, from June 2017 to May 2018 after approval from the Ethical Review Committee and College Of Physicians And Surgeons Pakistan. Total 370 patients with altered liver function Test (LFT) 16 to 40 years of age, primi and multiparous in all trimesters of pregnancies were included in this study. Patients with pre-existing liver disorders, hypertension, diabetes mellitus, and who have taken hepatotoxic medications in the past 6 months were excluded from the study. Nonprobability; consecutive sampling method was used. Data was collected by preformed structure Performa and analyzed on (SPSS) version 22.

**RESULTS:** The mean age of the patients was  $28.62 \pm 4.96$  years. Preeclampsia was the commonest reason for liver dysfunction during pregnancy, accounting for 48.1% of the cases followed by HELLP syndrome in 19.2%, acute fatty liver of pregnancy in 7.8%, Obstetric cholestasis accounted to 7% of the cases, and hyperemesis gravidarum 7.8% were found. Altered liver function are not directly related to pregnancy were Cholelithiasis (5.4%) and Viral Hepatitis (7%).

**CONCLUSION:** The prime reasons for abnormal liver function tests are pregnancy-related liver disorders. Prior and prompt combine care by the obstetric and gastroenterologist team can bring a beneficial impact in this so far disheartening situation in underdeveloped countries.

**KEYWORDS:** Liver dysfunction, Altered liver function test (LFT), hyperemesis gravidarum, cholelithiasis, Preeclampsia, Acute fatty liver, Obstetric cholestasis.

**INTRODUCTION**

Liver disorders during pregnancy are most prevalent than anticipated and possibly need specialized interventions<sup>1</sup>. It affects about 3% of all pregnancies<sup>2</sup>. Several physiological changes take place in sequence during pregnancy for the growth and structural development of a baby<sup>3</sup>. Liver physiology may change during pregnancy, which later on may progress to liver disease. The severity of the disease is related to morbidity and mortality<sup>4</sup>. Some liver diseases are specific to pregnancy like acute fatty liver of pregnancy (AFLP) and Intrahepatic cholestasis of pregnancy (IHCP), some are multi-systemic diseases with hepatic manifestations, for example, preeclampsia<sup>5</sup>, which is a widespread cause of maternal and perinatal mortality<sup>6</sup>.

Elevated liver enzymes can sometimes be encountered in asymptomatic pregnant women<sup>7</sup>, therefore an early diagnosis is important<sup>8</sup> for further assessment and accurate management<sup>9</sup>. The history and clinical examination provides valuable devices for distinguishing between un-pregnancy and pregnancy-related causes such as non-alcoholic fatty liver disease, acute viral infection, autoimmune liver disease, and Budd-Chiari syndrome. The natural path of liver functions may be affected by a pregnancy, for example, by an increased risk of hemorrhage due to acute viral hepatitis E infection and hepatocellular adenoma<sup>10</sup>.

Symptoms of liver dysfunction may differ according to the seriousness of liver injury from nausea, vomiting, fever, and abdominal pain to the signs of acute liver failure. Palmer erythema and spider angioma are usual physical examination findings in pregnancy, their presence may not specify underlying chronic liver disease<sup>11</sup>. Comprehension of pathogenesis and explanation of liver disease in pregnancy is nowadays advanced. A lot of classic diagnostic tests are available and many more are under research, despite that assessment for liver disease should begin with noninvasive testing<sup>12</sup>, which includes laboratory and radiographic studies. Laboratory investigations such as liver enzyme abnormalities and radiographic tests include conventional ultrasound of the liver. Further radiographic evaluation is needed; magnetic resonance imaging without contrast is bearable during pregnancy. Computed tomography in pregnancy must be carefully used due to the risks of ionizing radiation on the fetus. Invasive testing, such as liver biopsy and endoscopy, may be planned for proper management<sup>3</sup>.

The definition of abnormal liver function test pertained to value higher than normal range as defined by local laboratory (bilirubin > 24micro mol/l, alkaline phosphatase (ALP) >103 U/L, gamma-glutamyl transpeptidase (GGT) >26 U/L, (ALT) Alanine Aminotransferase or Serum glutamic – pyruvic transaminase (SGPT) > 51 U/L, Aspartate aminotransferase (AST) > 33 U/L<sup>17</sup>.

Prior diagnosis and timely decision for termination of pregnancy is the keystone of management. The life of the mother is the prime concern, hindrance in diagnosis and delivery may have adverse maternal and fetal outcomes.

This study will help us to know the burden of disease and will help us to understand in a better way the etiologies that affect our population. In the long run, it may help us to make protocols for early screening of common etiologies and thus lead to time management and a decrease in mortality.

**METHODOLOGY**

This Descriptive Cross-sectional study was conducted in the Department of Gynecology and Obstetrics, Liaquat University of Medical and Health Sciences, Jamshoro, Hyderabad from June 2017 to May 2018 after the Ethical approval from the College Of Physicians And Surgeons Pakistan. Total 370 pregnant women with altered liver function were included in this study. The sampling technique was Nonprobability, consecutive sampling. All pregnant ladies 16years to 40 years of age, primipara, multipara, grand multipara in all three trimesters with altered liver function tests, admitted to Obstetrics and gynecology unit at Liaquat University Hospital were included in this study. All Patients with known pre-existing liver disorders, hypertension, or diabetes mellitus and patients who have taken hepatotoxic medications during the past 6 months were excluded.

The aim of the study was explained to the patients and written informed consent was signed and relevant investigations were sent including Liver function test (LFT) blood sugar fasting, serum uric acid, Complete blood count (CBC), serum ammonia, serum creatinine, Prothrombin time (PT), International normalized ratio (INR) and serum lactate dehydrogenase (LDH) level. Ultrasound abdomen and pelvis was done, HBsAg, anti-HCV antibody, IgM for hepatitis A, and E were analyzed. The data was collected on preformed structure Performa and analyzed on (SPSS) version 22. For qualitative data, booking status and outcome [Acute fatty liver, Hemolysis elevated liver enzymes and low platelet syndrome (HELLP), obstetric cholestasis, pre-eclampsia, hyperemesis, gravidam, cholelithiasis, viral hepatitis] were expressed as frequency and percentage. For quantitative data (age, parity, gravida, and gestational age) mean and standard deviation were calculated.

Stratification of outcome variable was done in view to age groups, parity, gravida, gestational week of pregnancy, parity, and booking status. Post-stratification Chi-square test was applied to see the effect of on outcome. P-value 0.05 was taken as statistically significant.

**RESULTS**

In this research total of 370 pregnant women with altered liver function tests were included. Some physiologic characteristics are shown in **Table I**. The average age of the patients was 28.62±4.96 years, likewise, the average gestational age was 38.42 weeks, gravida 2.83, and parity 1.83 are revealed from **Table I**. The frequency for etiology of altered liver function in pregnancy is presented in **Table II**. Preeclampsia was the commonest reason for liver dysfunction during pregnancy, accounting for 48.1% of the cases followed by HELLP syndrome in 19.2%, acute fatty liver of pregnancy 7.8%, Obstetric cholestasis accounted to 7% of the cases, hyperemesis gravidarum 7.8%. Altered liver functions not directly related to pregnancy were Cholelithiasis 5.4% and Viral Hepatitis 7%.

Stratification analysis concerning gestational age and parity was performed and presented in **Table III**. Liver dysfunction due to pre-eclampsia, HELP syndrome, and obstetric cholestasis were more common in primigravidas than multigravida women. Only cholelithiasis was found to be significantly varied 3 groups of parity. We did not find any significant difference for any of the etiological factors between 36-37 and more than 38 weeks except pre-eclampsia and acute fatty liver of pregnancy. (**Table III**)

**TABLE I: PHYSIOLOGIC CHARACTERISTICS IN A PREGNANT WOMAN**

<b>Variables</b>	<b>Mean ±SD</b>	<b>95 % Confidence Interval</b>
Age (Years)	28.62±4.96	28.11-29.13
Gestational Age (Weeks)	38.42±1.12	38.30-38.53
Gravida	2.83±1.13	2.72-2.95
Parity	1.83±1.13	1.72-1.95

**TABLE II: FREQUENCY FOR ETIOLOGY OF ALTERED LIVER FUNCTION IN PREGNANCY**

<b>Etiology Of Altered Liver Function</b>	<b>Frequency</b>	<b>Percentage</b>
Acute Fatty Liver of Pregnancy	29	7.8%
HELLP	71	19.2%
Obstetric Cholestasis	26	7%
Pre-eclampsia	178	48.1%
Hyperemesis gravidarum	28	7.6%
Cholelithiasis	20	5.4%
Viral Hepatitis	26	7%

**TABLE III: FREQUENCY FOR ETIOLOGY OF ALTERED LIVER FUNCTION IN PREGNANCY BY GESTATIONAL AGE & PARITY**

Etiology Of Altered Liver Function	Gestational age (Weeks)		P-Value	Parity			P-Value <0.05
	36-37 n=228	≥38 n=142		Primi n=203	Multi n=148	Grand multi n=19	
Acute Fatty Liver of Pregnancy	20(8.8%)	9(6.3%)	0.397	15(7.4%)	12(8.1%)	2(10.5%)	0.877
HELLP	41(18%)	30(21.1%)	0.455	41(20.2%)	28(18.9%)	2(10.5%)	0.589
Obstetric Cholestasis	15(6.6%)	11(7.7%)	0.669	19(9.4%)	7(4.7%)	0(0%)	0.115
Pre-eclampsia	111(48.7%)	67(47.2%)	0.779	105(51.7%)	64(43.2%)	9(47.4%)	0.291
Hyperemesis gravidarum	14(6.1%)	14(9.9%)	0.188	20(9.9%)	8(5.4%)	0(0%)	0.131
Cholelithiasis	14(6.1%)	6(4.2%)	0.428	1(0.5%)	15(10.1%)	4(21.1%)	0.0005
Viral Hepatitis	18(7.9%)	8(5.6%)	0.408	9(4.4%)	16(10.8%)	1(5.3%)	0.066

## DISCUSSION

Pregnancy is characterized by numerous physiological changes that may lead to a diversity of gastrointestinal symptoms raising the challenge for both gastroenterologists and obstetricians<sup>13</sup>. Genuine interpretation of abnormal liver function test is required to avoid misdiagnosis.<sup>14</sup> Younger age group has a higher prevalence of liver dysfunction. Our research shows the majority of women from 26-30 years of age (Table –I). The average age of the patients was 28.62±4.96 years. The majority of the women was un-booked in our study for antenatal care and generally got admitted through the emergency department or referred from rural areas and secondary care hospitals. Similar facts are observed in the study conducted by Ling Yi C 2011<sup>15</sup> and Nagaria T 2005<sup>16</sup>.

Most studies describe the source of abnormal LFT as pregnancy-related and range from 67 to 89 %<sup>17,18</sup>. Hypertensive disorders of pregnancy that involve the liver include preeclampsia/eclampsia and HELLP syndrome. Preeclampsia is seen in about 3% to 5% of pregnancies, hepatic dysfunction with preeclampsia is acknowledged for a long time<sup>19</sup>. Three to 10 percent of patients with preeclampsia may progress towards HELLP syndrome and accounts for 0.1 percent of all pregnancies<sup>20,21</sup>. In this research Preeclampsia was the most common cause of altered liver function in pregnancy calculating 48.1% cases followed by HELLP syndrome in 19.2% cases (**Table II**). It often develops in the second half of pregnancy in genetically prone individuals<sup>22</sup>. The incidence of intrahepatic cholestasis of pregnancy varies from 0.1 to 1.5 % of pregnancies<sup>23</sup>, 7% of the woman had intrahepatic cholestasis of pregnancy in our study. In contrast, one Pakistani study conducted in Rawalpindi had a very low incidence of 0.4%<sup>24</sup>. Another study conducted by Ambros-Rudolph, the incidence was 2% but the main concerns were the cutaneous lesions as it was done by dermatologists<sup>22</sup>.

Acute fatty liver of pregnancy is an infrequent, certainly lethal disease, characterized by microvesicular fatty infiltration of the liver leading to multiorgan failure. Because of the potential for rapid progression to coma and death, AFLP is considered to be an obstetrics emergency<sup>25</sup>. It affects 1 in 7000 to 16,000 pregnancies<sup>26</sup>. One study conducted by Knight et al in the UK showed the incidence of AFLP was 5 cases per 100 000 maternities<sup>27</sup>. On the other hand our study is dissimilar from the above results and has shown that altered liver function in pregnancy is amazingly common. We found the frequency of AFLP was 7.8% as an etiology of altered liver function in pregnancy. Hyperemesis Gravidarum is a brutal form of Nausea and vomiting of pregnancy. In one series, hyperemesis gravidarum accounted for 32% of liver function test abnormalities among pregnant women of all gestational ages, 7.8% of patients in our study showed hyperemesis gravidarum as an etiology of altered liver function in pregnancy. Viral hepatitis is very common in developing countries; on the other hand, hepatitis E is associated with fulminant hepatic failure in pregnancy<sup>28</sup>.

The evaluation and treatment of viral hepatitis during pregnancy need exceptional consideration. All five liver-specific viruses (hepatitis A, B, C, D, E) each have individual epidemiology and likelihood to progress towards chronic liver disease or other complications.<sup>29</sup> We did not find any significant difference for any of the etiological factors between 36-37 and more than 38 weeks except preeclampsia and acute fatty liver of pregnancy. (**Table III**) Cholelithiasis is found in about 6 percent of pregnant ladies. Pregnancy, multiparity, and obesity are the risk factors of cholelithiasis<sup>30</sup>. In our study, 5.4% of women had Cholelithiasis as a cause of altered liver function not directly related to pregnancy. Cholelithiasis was found significantly varied in 3 groups of parity.

## **CONCLUSION**

The prime source of altered liver function tests is pregnancy-related disorders. Women with preeclampsia or HELLP syndrome are at higher risk for peri and postpartum complications, with consecutive comorbidities. Despite research and advancement in medical care, maternal and fetal outcomes are not gratifying. A structured approach, prior and prompt multidisciplinary care can bring bright results in the developing world.

**Conflict of Interest:** There is *no* conflict of *interest among the authors*.

**Financial Disclosure / Grant Approval:** There was no funding agency.

**DATA SHARING STATEMENT:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions

## **AUTHOR CONTRIBUTIONS**

Najam H: Primary investigator, Data collection

Memon FP: Introduction

Naeem S: Results

Memon A: Discussion



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