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Original Research Article

THE IMPACT OF ELEVATED LIVER ENZYMES AND İNTRAHEPATIC CHOLESTASIS OF PREGNANCY ON THE COURSE OF COVID-19 IN PREGNANT WOMEN

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Abstract: *COVID-19 in pregnancy presents unique challenges, particularly in the presence of liver dysfunction, including elevated liver enzymes and intrahepatic cholestasis of pregnancy (ICP). These conditions may worsen the disease course and contribute to adverse maternal and fetal outcomes.* ***Objective:*** *To evaluate the impact of elevated liver enzymes and intrahepatic cholestasis of pregnancy (ICP) on the clinical course, severity, and outcomes of COVID-19 in pregnant women.* ***Methods:*** *A retrospective cohort study was conducted at Punjab Medical College Faisalabad during June 2024 to October 2024. A total of 500 pregnant women diagnosed with COVID-19 were included in the study. The patients were divided into three groups: (1) COVID-19 patients with normal liver function, (2) COVID-19 patients with elevated liver enzymes, and (3) COVID-19 patients with ICP. Liver function tests, clinical outcomes, and maternal and fetal complications were analyzed. Statistical comparisons were made to assess the severity of COVID-19 symptoms and outcomes across these groups.* ***Results:*** *Data were collected from 500 patients, with no significant differences in age (31.4 ± 5.2 years vs. 30.8 ± 4.9 years, p = 0.24), gestational age at diagnosis (26.5 ± 4.1 weeks vs. 27.1 ± 3.8 weeks, p = 0.18), pre-pregnancy BMI (26.3 ± 4.5 vs. 25.8 ± 4.1, p = 0.15), or comorbidities such as diabetes (18% vs. 16.8%, p = 0.57) and hypertension (12% vs. 11.2%, p = 0.73). However, clinical outcomes differed significantly between the groups. The liver dysfunction group had a higher hospitalization rate (72%, 180/250 vs. 48%, 120/250, p < 0.001) and a greater proportion of ICU admissions (22%, 40/250 vs. 12.5%, 15/250, p = 0.02).* ***Conclusion:*** *Elevated liver enzymes and ICP in pregnant women significantly worsen the clinical course and outcomes of COVID-19. These conditions are associated with increased risks of severe maternal complications, adverse fetal outcomes, and the need for intensive medical care. Early detection and management of liver dysfunction in pregnant women with COVID-19 are critical for improving outcomes.*

Keywords: COVID-19, pregnancy, liver enzymes, intrahepatic cholestasis, maternal outcomes, fetal outcomes

Introduction

The COVID-19 pandemic has profoundly impacted global health systems, exposing many vulnerabilities across various demographics. The unique hormonal changes and immune modifications during pregnancy create additional challenges for managing COVID-19 while maintaining pregnancy health outcomes for vulnerable expectant mothers (1). Liver function remains sensitive to pregnancy-related alterations in immunologic responses, hormonal balances, and changes in the fetal and maternal immune systems. When Pregnancy occurs, liver enzyme elevations merge with the appearance of intrahepatic cholestasis of pregnancy (ICP) as liver conditions that produce severe dangers for maternal and fetal outcomes (2). Medical experts have found that these conditions contribute to worsening both the respiratory and systemic effects that COVID-19 causes by affecting multiple vital organs, including the liver (3).

Pregnant women showing elevated liver enzymes in their blood can have different underlying medical conditions that range from benign enzyme abnormalities of gestational origin to serious complications, including preeclampsia or HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) (4). The combination of elevated transaminases reveals liver damage that worsens in viral infections, increasing the likelihood of severe complications. When ICP, a bile acid metabolism disorder, affects pregnant women, it intensifies the COVID-19 impact on them. Plasma levels of bile acids become elevated in ICP, which results in itchy skin conditions with liver yellowing and puts mothers at risk for poor pregnancy outcomes like premature delivery and babies experiencing breathing problems or stillbirth (5).

The interaction of these liver disorders with the recent SARS-CoV-2 virus represents a vital area for scientific investigation. Understanding the related effects may advance better care methods for mothers and improve birth outcomes (6). Thus far, research has paid attention to how COVID-19 affects the lungs and cardiovascular systems, but recent studies suggest it directly impacts liver function. People infected with SARS-CoV-2 exhibit elevated liver enzyme levels because the infection commonly causes actual liver damage or functional impairments (7). Existing liver conditions in pregnant people stand to intensify COVID-19-related medical consequences while raising the risk of severe conditions, including liver failure, coagulopathy, and sepsis (8). Women carrying a child have an increased risk of preterm labor and fetal growth

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restriction along with preeclampsia when they have higher liver enzyme levels or ICP. The dangers of inflammatory response from COVID-19 become more severe when these conditions exist together (9). These patients suffer impaired medication metabolism due to liver dysfunction, which makes COVID-19 treatment medicine incompatible with their condition. Maternal liver dysfunction risks rising, which potentially leads to fetal distress that requires increased monitoring accompanied by earlier medical interventions (10). The clinical management of ICP alongside elevated liver enzymes in COVID-19 patients demands tortuous management through effective teamwork between obstetricians working together with hepatologists and infectious disease specialists (11). The COVID-19 pandemic has created an immediate need to revise clinical protocols to manage patients with concurrent health problems while protecting maternal and fetal health through disease treatment. Future development should focus on improving pregnancy-specific liver dysfunction diagnostic standards, monitoring systems, and well-defined treatment protocols that target viral infection management alongside liver-related problems (12).

Objective

To evaluate the impact of elevated liver enzymes and intrahepatic cholestasis of pregnancy (ICP) on the clinical course, severity, and outcomes of COVID-19 in pregnant women.

Methodology

This retrospective study was conducted at Punjab Medical College Faisalabad during June 2024 to October 2024. A total of 500 pregnant women were included in the study. Pregnant women aged 18 to 45 years who tested positive for SARS-CoV-2 via PCR or antigen testing. A diagnosis of elevated liver enzymes (AST, ALT, alkaline phosphatase) or ICP during pregnancy. Women who were hospitalized during their pregnancy due to COVID-19.Pregnant women with pre-existing chronic liver diseases (e.g., cirrhosis, chronic hepatitis).Women with multiple gestations. Patients who were lost to follow-up or did not complete the study period. Patient data were collected from medical records, which included demographic information, clinical presentation, laboratory results, and pregnancy outcomes. Demographic characteristics include age, pre-pregnancy body mass index (BMI), and comorbid conditions like diabetes and hypertension, which could affect both COVID-19 outcomes and pregnancy health. Laboratory results, including liver function tests (AST, ALT, alkaline phosphatase) and bile acid levels, were analyzed to assess the presence and severity of liver dysfunction. Pregnancy-related outcomes were also noted, including the occurrence of complications like preeclampsia, gestational hypertension, preterm labor, and fetal outcomes, such as birth weight and Apgar scores. Data were analyzed using SPSS v26. Multivariate logistic regression models were then used to control for potential confounders, such as maternal age, gestational age at diagnosis, and pre-existing comorbidities, and to assess the independent effects of liver dysfunction on COVID-19 severity, the need for ICU admission, and pregnancy complications.

Results

Data were collected from 500 patients, with no significant differences in age (31.4 ± 5.2 years vs. 30.8 ± 4.9 years, p = 0.24), gestational age at diagnosis (26.5 ± 4.1 weeks vs. 27.1 ± 3.8 weeks, p = 0.18), pre-pregnancy BMI (26.3 ± 4.5 vs. 25.8 ± 4.1, p = 0.15), or comorbidities such as diabetes (18% vs. 16.8%, p = 0.57) and hypertension (12% vs. 11.2%, p = 0.73). However, clinical outcomes differed significantly between the groups. The liver dysfunction group had a higher hospitalization rate (72%, 180/250 vs. 48%, 120/250, p < 0.001) and a more significant proportion of ICU admissions (22%, 40/250 vs. 12.5%, 15/250, p = 0.02).

The mean ALT level was 75.2 ± 18.3 U/L in the liver dysfunction group, compared to 25.6 ± 8.3 U/L in the control group (p < 0.001). Similarly, the mean AST level was also significantly higher in the liver dysfunction group (68.4 ± 22.1 U/L) compared to the control group (26.3 ± 7.4 U/L, p < 0.001). Additionally, bile acid elevation was observed in 28% (70/250) of women in the liver dysfunction group, whereas no cases were reported in the control group (0%, p < 0.001).

In terms of pregnancy outcomes, the liver dysfunction group showed higher rates of preterm birth (18%, 45/250 vs. 11.2%, 28/250, p = 0.03) and fetal distress (12.4%, 31/250 vs. 7.6%, 19/250, p = 0.04) compared to the control group. The mean gestational age at delivery was also lower in the liver dysfunction group (37.2 ± 2.4 weeks vs. 38.1 ± 1.9 weeks, p = 0.02), suggesting a higher incidence of premature births. Neonatal outcomes were slightly worse in the liver dysfunction group, with lower mean Apgar scores at both 1 minute (8.1 ± 1.4 vs. 8.5 ± 1.1, p = 0.05) and 5 minutes (9.2 ± 1.0 vs. 9.4 ± 0.7, p = 0.05), although these differences were modest. The stillbirth rate was slightly higher in the liver dysfunction group (1.2%, 3/250 vs. 0.8%, 2/250), but this difference was not statistically significant (p = 0.35).

The odds of ICU admission were 2.6 times greater in the liver dysfunction group (OR = 2.6, 95% CI: 1.4 – 4.9, p = 0.02). Similarly, the likelihood of preterm birth was increased by 1.6 times (OR = 1.6, 95% CI: 1.1 – 2.5, p = 0.04). However, the odds of requiring mechanical ventilation were not significantly different between the two groups (OR = 1.2, 95% CI: 0.8 – 1.9, p = 0.21), indicating no strong association between liver dysfunction and the need for mechanical support.

Regarding treatment, the majority of both groups received standard COVID-19 care, with 88% (220/250) of the liver dysfunction group and 92% (230/250) of the control group receiving the same (p = 0.24). However, a significant difference was observed in the use of modified medications, as 18% (45/250) of the liver dysfunction group received adjustments to their treatment regimen, compared to none in the control group (0%, p < 0.001).

Table 1: Baseline Characteristics of Study Participants

Characteristic	Liver Dysfunction Group (n = 250)	Control Group (n = 250)	p-value
Age (mean ± SD)	31.4 ± 5.2	30.8 ± 4.9	0.24
Gestational Age at Diagnosis (weeks)	26.5 ± 4.1	27.1 ± 3.8	0.18
Pre-pregnancy BMI (mean ± SD)	26.3 ± 4.5	25.8 ± 4.1	0.15

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Comorbidities (n, %)			
- Diabetes	45 (18%)	42 (16.8%)	0.57
- Hypertension	30 (12%)	28 (11.2%)	0.73
Outcome	Liver Dysfunction Group (n = 250)	Control Group (n = 250)	p-value
Hospitalized (n, %)	180 (72%)	120 (48%)	< 0.001
ICU Admission (n, %)	40 (22%)	15 (12.5%)	0.02
Mean Duration of Hospitalization (days)	9.4 ± 3.2	6.7 ± 2.3	< 0.001

Table 2: Liver Function Test Results

Liver Function Test	Liver Dysfunction Group (n = 250)	Control Group (n = 250)	p-value
Mean ALT (U/L)	75.2 ± 18.3	25.6 ± 8.3	< 0.001
Mean AST (U/L)	68.4 ± 22.1	26.3 ± 7.4	< 0.001
Bile Acid Elevation (n, %)	70 (28%)	0 (0%)	< 0.001

Table 3: Pregnancy Outcomes

Outcome	Liver Dysfunction Group (n = 250)	Control Group (n = 250)	p-value
Preterm Birth (n, %)	45 (18%)	28 (11.2%)	0.03
Mean Gestational Age at Delivery (weeks)	37.2 ± 2.4	38.1 ± 1.9	0.02
Fetal Distress (n, %)	31 (12.4%)	19 (7.6%)	0.04
Mean Apgar Score at 1 minute (mean ± SD)	8.1 ± 1.4	8.5 ± 1.1	0.05
Mean Apgar Score at 5 minutes (mean ± SD)	9.2 ± 1.0	9.4 ± 0.7	0.05
Stillbirth (n, %)	3 (1.2%)	2 (0.8%)	0.35

Table 4: Multivariate Analysis of Severe COVID-19 Outcomes

Outcome	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
ICU Admission	2.6	1.4 – 4.9	0.02
Preterm Birth	1.6	1.1 – 2.5	0.04
Mechanical Ventilation	1.2	0.8 – 1.9	0.21

Table 5: Treatment and Management

Treatment	Liver Dysfunction Group (n = 250)	Control Group (n = 250)	p-value
Received Standard COVID-19 Care (n, %)	220 (88%)	230 (92%)	0.24
Modified Medications (n, %)	45 (18%)	0 (0%)	< 0.001
Additional Liver Treatments (n, %)	62 (24.8%)	0 (0%)	< 0.001

Discussion

This study aimed to investigate the impact of elevated liver enzymes and intrahepatic cholestasis of pregnancy (ICP) on the clinical course of COVID-19 in pregnant women. The research shows that pregnant patients with liver dysfunction, particularly those diagnosed with ICP developments, experience significantly worse COVID-19 outcomes, leading to higher hospitalization rates, extended hospital durations, and increased need for ICU admissions over pregnant patients without liver conditions (13). The study revealed that liver dysfunction during pregnancy led to a Hospitalization rate of 72%, whereas normal pregnant women experienced hospitalization at 48%. Research shows that liver dysfunction combined with pregnancy makes both conditions more prone to experiencing serious infections as well as more serious health complications (14). People with liver enzyme elevation demonstrate hepatic stress, which reduces immune response and worsens COVID-19 disease severity. Hospitalization times were significantly longer for women with liver dysfunction, who spent an average of 9.4 days in medical care compared to 6.7 days for participants in our control group. This data underscores the worse burden of liver dysfunction through viral infections (15).

The necessity for intensive care services showed a significant difference between high-risk patients at 22% and the control group receiving 12.5% care. A higher need for specialized medical treatment seems to reveal a weakened maternal immune response and disturbed metabolic processes that pregnancy may already affect. Multiple contributors create the elevated risk profile (16). The negative effects of liver dysfunction on detoxification, immune protein synthesis, and medication metabolism create challenges for treating and recovering from COVID-19. Our research supports that liver dysfunction leads to recognized unfavorable pregnancy results. Laboratory testing confirmed preterm delivery occurred at a higher rate among women with liver dysfunction (18%) compared to those without liver dysfunction (11.2%) (17). Studies confirm that raised liver enzyme levels alongside elevated ICP both lead to higher preterm labor and fetal growth restriction risk while causing multiple obstetric problems. Small for gestational age concept considers liver dysfunction, specifically ICP, as a cause of modified inflammatory response that leads to premature uterine

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contractions in expectant mothers. The combination of viral infection and hepatic injury produces elevated inflammatory cytokines in the bloodstream, intensifying the risk of premature birth (18).

Liver dysfunction-related fetal outcomes showed unfavorable patterns when researchers compared the liver dysfunction group to controls as their measurements revealed increased fetal distress rates (12.4% vs. 7.6%) alongside lower 1-minute Apgar scores (8.1 vs. 8.5). Lab analysis revealed significant differences between test groups in Apgar scores at birth but every infant exceeded basic health measurements across both populations. Nevertheless, the association between liver dysfunction and poorer neonatal outcomes, particularly in the context of COVID-19, underscores the importance of close monitoring of both maternal and fetal health in this high-risk population (19). Pregnant subjects displaying liver dysfunction demonstrated marked increases in liver enzymes ALT and AST, according to our analysis. Liver dysfunction patients showed significantly elevated ALT and AST levels at 75.2 U/L and 68.4 U/L, respectively, whereas control participants demonstrated lower measurements at 25.6 U/L and 26.3 U/L. Research supports these results since multiple studies show that COVID-19 liver damage leads to liver enzyme elevations when individuals with SARS-CoV-2 infection are tested (20). Patients with pre-existing liver conditions who become pregnant face an increased risk of developing complications such as coagulopathy, bleeding, and liver failure following liver damage. The hepatic malady ICP causes bile acid build-up that disrupts liver elimination functions, thus complicating the treatment of COVID-19 disease. This study illustrates that pregnant women who have liver dysfunctions need better monitoring combined with custom healthcare strategies throughout the COVID-19 pandemic (21). The profound adverse birth outcomes demonstrated in the liver dysfunction group prove that these pregnant women need additional rigorous hospital-based management. The practice of closely monitoring liver function stands essential for clinicians attending pregnant women with elevated liver enzymes or ICP both before and after SARS-CoV-2 testing because COVID-19 typically intensifies baseline liver problems. This population requires medication management adjustments targeting COVID-19 treatment considerations for their distinct pharmacological changes and liver damage potential. The long hospital stays combined with the increased severity of illness require immediate detection strategies to reduce potential complications from COVID-19 disease progression. Complex pregnancy management demands active participation from healthcare experts specializing in maternal-fetal care and expertise in hepatology and infectious diseases. Multiple limitations exist in this study which nonetheless delivers important intelligence about liver-function effects and pregnant women undergoing COVID-19 impacts. The study design as a retrospective analysis lacks methodological strength for identifying cause-effect relationships and grouping across various institutions, leading to inconsistent patient care.

Conclusion

It is concluded that elevated liver enzymes and intrahepatic cholestasis of pregnancy (ICP) significantly worsen the clinical course of COVID-19 in pregnant women. Our study found that women with liver dysfunction had higher hospitalization rates, longer stays, increased ICU admissions, and a greater likelihood of preterm birth compared to those without liver abnormalities.

Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned.

Consent for publication
Approved

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Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

ANDLEEB KANWAL (Medical Officer)
Coordination of collaborative efforts.
Study Design, Review of Literature.
SHEEMA KHAN (Assistant professor)
Conception of Study, Development of Research manuscript Review, and final approval of manuscript.
Conception of Study, Final approval of manuscript.
ALINA MUNEEB (Consultant Physician)
Manuscript revisions, critical input.
Coordination of collaborative efforts.
Data acquisition and analysis.
Manuscript drafting.

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