International Journal of Gynaecology and Obstetrics Research
www.gynaecologyjournal.in
E-ISSN: 2663-3612
Received: 22-03-2026, Accepted: 18-03-2026, Published: 10-04-2026
Volume 8, Issue 2, 2026, Page No. 45-50

Association of serum il-6 and tnf-α levels with intrahepatic cholestasis of pregnancy

Dr. Aishwarya[1], Dr Geeta Yadav[2], Mohsin Ali Khan[3], Dr. Uma Gupta[4], Dr. Priti Vatsal[4], Dr. S P Jaiswar[5]

[1] Department of Obstetrics & Gynaecology, Era's Lucknow Medical College & Hospital, Lucknow, Uttar Pradesh, India

[2] Associate Professor, Department. of Obst & Gynecolgy, Era's Lucknow Medical College, Sarfarganj, Hardoi Road, Lucknow, Uttar Pradesh, India

[3] Hon'ble Chancellor, Era university Era's Lucknow Medical College, Sarfarganj, Hardoi Road, Lucknow, Uttar Pradesh, India

[4] Professor, Department of Obstetrics & Gynaecology Era's Lucknow Medical College & Hospital, Lucknow, Uttar Pradesh, India

[5] Associate Professor & Head Department of Obstetrics & Gynaecology Era's Lucknow Medical College & Hospital, Lucknow, Uttar Pradesh, India

Corresponding Author: Dr. Uma Gupta

Abstract

Background: Intrahepatic cholestasis of pregnancy (ICP) is associated with adverse perinatal outcomes. Measurement of total bile acid (TBA) levels is most reliablel test. With growing interest in the inflammatory basis of ICP, the present study was undertaken to evaluate the association of inflammatory markers serum IL-6 and TNF-α levels with liver enzyme levels in women with ICP.

Objective: To measure levels of alanine transaminase (ALT) and aspartate transaminase (AST) and and TNF alpha in women with obstetric cholestasis and controls and find if there any association

Methods: This was a hospital-based case–control study to evaluate the association of serum IL-6 and TNF-α levels with liver enzyme levels in ICP cases and controls. ICP was confirmed by clinical as well as total bile acid level levels >10 µmol/L; ALT and/or AST, Interleukin-6 (IL-6) Tumor Necrosis Factor-alpha (TNF-α) were estimated using enzyme-linked immunosorbent assay (ELISA) kits. Statistical Analysis was done as required.

Results: There were 84 participants with 42 in each group. Mean ALT and AST were raised in cases, $p < 0.001$). A gradual increase in IL-6 and TNF-α levels was observed with increasing AST, ALT, and total bile acids among women with ICP. The levels were in increasing trends However, the differences between categories were not statistically significant ($p > 0.05$).

Conclusion: In conclusion, the present study demonstrates that although liver enzymes (ALT and AST) are significantly elevated in women with intrahepatic cholestasis of pregnancy, serum IL-6 and TNF-α levels do not show a significant association with hepatic enzyme levels or disease severity.

Keywords: Inflammatory markers, serum Il-6 and tnf-alpha levels with intrahepatic cholestasis of pregnancy

Introduction

Intrahepatic cholestasis of pregnancy (ICP) is a liver disorder that occurs exclusively during pregnancy. Its incidence varies geographically and demonstrates familial clustering as well as recurrence in subsequent pregnancies [1]. Measurement of total bile acid (TBA) levels is considered the most reliable and widely used biochemical test for diagnosing ICP, and elevation of TBA may be the earliest detectable laboratory abnormality [2]. Serum TBA levels can fluctuate and generally increase as pregnancy advances. major concern in ICP lies in its association with adverse perinatal outcomes, including preterm birth, fetal distress, and an increased risk of intrauterine fetal demise [3]. Researchers found significantly elevated levels of high sensitivity C-reactive protein (hs-CRP), Interleukin -6(IL-60, and Tumor Necrosis Factor-α(TNF-α) in women with ICP compared to controls [4]. Biberoglu *et al*. observed that serum IL-6 levels were significantly higher in both mild and severe ICP groups relative to controls, although hs-CRP levels did not differ significantly [5]. Yu *et al*. demonstrated increased levels of IL-12, IL-18, and TNF-α in ICP patients [6]. Additionally, IL-17 [7] and IL-31[8] have been reported to be significantly elevated in ICP. Shao *et al*. found that IL-18, IL-12, and TNF-α levels were significantly higher in severe ICP compared to mild ICP, while no significant difference was noted between mild ICP and healthy controls [9].

Despite growing interest in the inflammatory basis of ICP, current evidence remains inconsistent and inconclusive. Furthermore, limited research has specifically examined the association between pro-inflammatory cytokines such as IL-6 and TNF-α and biochemical markers of hepatic dysfunction in ICP. This lack of clarity highlights an important research gap in understanding whether systemic inflammation contributes to the pathophysiology of ICP. Therefore, the present study was undertaken to evaluate the association of serum IL-6 and TNF-α levels with liver enzyme levels in women with intrahepatic cholestasis of pregnancy, with the aim of providing further insight into the inflammatory mechanisms underlying this condition.

Objectives

1. To measure levels of alanine transaminase (ALT) and aspartate transaminase (AST) in women with obstetric cholestasis.
2. To measure levels of IL-6 and TNF alpha in women with obstetric cholestasis and controls.

3. To determine if there is any association between ALT, AST levels with IL-6 and TNF alpha.

Material and Methods

Study Design

This was a hospital-based analytical case–control study conducted to evaluate the association of serum IL-6 and TNF-α levels with liver enzyme levels in women diagnosed with intrahepatic cholestasis of pregnancy (ICP).

Study Setting

The study was conducted in the Department of Obstetrics and Gynaecology, Era's Lucknow Medical College and Hospital, Lucknow.

Study Duration

The study was conducted over 24 months

Study Population

The study population included pregnant women attending the antenatal outpatient department and admitted to the labor ward during the study period.

Two groups were included

Cases: Pregnant women diagnosed with intrahepatic cholestasis pregnancy (ICP).
Controls: Healthy pregnant women without ICP, matched for gestational age.

Sample Size

A total of 84 participants were included in the study, comprising:

- **Group 1 [Cases]:** Pregnant women with obstetric cholestasis
- **Group 2 [Controls]:** Age matched healthy pregnant women

The sample size was determined based on previous literature and feasibility during the study period.
n = 42 each group

Group 1[Cases]

Inclusion criteria

- Age 19–40 years
- Gestation ≥ 14 weeks
- Singleton pregnancy
- Pregnancies with Obstetric cholestasis

Exclusion criteria

- Stillborn baby
- Major congenital anomalies in baby
- Dermatological conditions for pruritis
- Viral hepatitis
- HELLP (Haemolysis, elevated liver enzymes, low platelet count) syndrome
- Acute fatty liver of pregnancy
- Obstructive jaundice

Group 2 [Controls]

Inclusion criteria

- 19–40 years
- Singleton Pregnancies
- ≥ 14 weeks
- uncomplicated by medical disorders

Exclusion criteria

- Stillborn baby
- Major congenital anomalies in baby
- Dermatological conditions for pruritis
- Viral hepatitis
- HELLP (Haemolysis, elevated liver enzymes, low platelet count) syndrome
- Acute fatty liver of pregnancy
- Obstructive jaundice

Diagnostic Criteria for ICP

Diagnosis of intrahepatic cholestasis of pregnancy was based on:

- Presence of generalized pruritus.
- Elevated fasting serum total bile acid (TBA) levels >10 μmol/L.
- Elevated liver enzymes (ALT and/or AST).
- Resolution of symptoms and normalization of laboratory parameters after delivery.

Severity of ICP was classified based on TBA levels

- **Mild:** 19–39 μmol/L
- **Moderate:** 40–99 μmol/L
- **Severe:** ≥100 μmol/L

Data Collection Procedure

After obtaining written informed consent, detailed history and clinical examination were performed. Data collected included:
Age, parity, gestational age, presence of pruritus, associated symptoms (e.g., loss of appetite), anthropometric measurements (weight, height, BMI) BMI was calculated using the formula: BMI = Weight (kg) / Height (m^2)

Laboratory Investigations

Venous blood samples were collected under aseptic precautions.

The following parameters were measured

Liver Function Tests

- Alanine aminotransferase (ALT)
- Aspartate aminotransferase (AST)

These were measured using automated biochemical analyzer methods.

Serum Total Bile Acid (TBA)

Measured using enzymatic assay method.

Inflammatory Markers

- Interleukin-6 (IL-6)
- Tumor Necrosis Factor-alpha (TNF-α)

These were estimated using enzyme-linked immunosorbent assay (ELISA) kits according to manufacturer instructions.
All samples were processed in the central laboratory under standardized conditions.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 21.0.

- Continuous variables were expressed as mean ± standard deviation (Mean ± SD).
- Categorical variables were expressed as frequency and percentage.
- Independent t-test was used to compare means between two groups.

- Pearson correlation analysis was used to assess relationships between variables.
- Multivariable linear regression analysis was performed to evaluate independent associations.
- A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after approval from the Institutional Ethics Committee of Era's Lucknow Medical College and Hospital. Written informed consent was obtained from all participants. Confidentiality of patient data was strictly maintained throughout the study.

Results

The present case–control study was conducted to evaluate the association of serum IL-6 and TNF-α levels with liver enzyme levels in women diagnosed with intrahepatic cholestasis of pregnancy (ICP). A total of 84 participants were included, comprising 42 cases (women with obstetric cholestasis) and 42 healthy pregnant controls matched for age and parity.

Table 1: Age-wise Distribution of Study Participants Among Women with Obstetric Cholestasis (Cases) and Healthy Pregnant Women (Controls)

Age group (years)	Cases (n = 42) n (%)	Controls (n = 42) n (%)
19–25	10 (23.8%)	9 (21.4%)
26–30	18 (42.9%)	19 (45.2%)
31–35	10 (23.8%)	13 (31.0%)
36–40	4 (9.5%)	1 (2.4%)
Total	42 (100)	42 (100)

This table shows the age-wise distribution of study participants among cases and controls. The majority of participants in both groups belonged to the 26–30 years age group [Table 1].

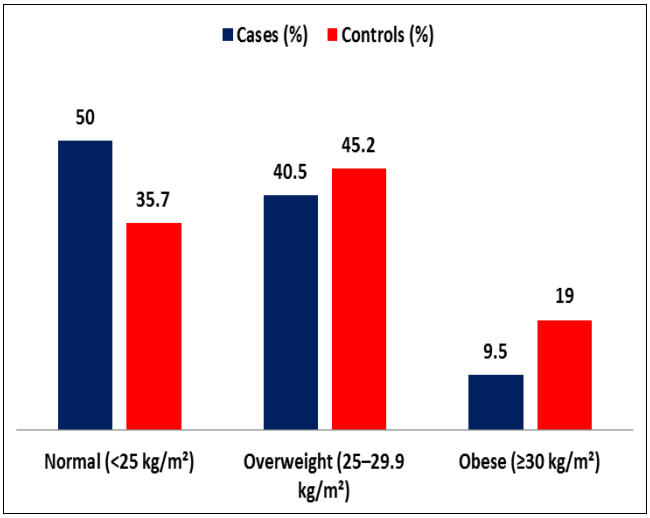

Fig 1: Body Mass Index Distribution Among Women with Obstetric Cholestasis (Cases) and Healthy Pregnant Women (Controls) (n = 84).

Fig 1. shows the BMI distribution among cases and controls. Among cases (n = 42), 21 (50.0%) had normal BMI (<25 kg/m²), 17 (40.5%) were overweight (25–29.9 kg/m²), and 4 (9.5%) were obese (≥30 kg/m²). Among controls (n = 42), 15 (35.7%) had normal BMI, 19 (45.2%) were overweight, and 8 (19.0%) were obese. Obesity was higher among controls compared to cases.

Pruritus was present in 40 (95.2%) cases and absent in 2 (4.8%) cases, indicating that pruritus was the predominant symptom.

Table 2: Comparison of Maternal Clinical and Anthropometric Parameters Between Women with Obstetric Cholestasis (Cases) and Healthy Pregnant Women (Controls).

Parameter	Cases (Mean ± SD) n-42	Controls (Mean ± SD) n-42	t-value	p-value
Age (years)	29.6 ± 3.2	30.2 ± 3.0	-0.83	0.409
Gestation (weeks)	34.9 ± 2.1	38.6 ± 1.1	-9.74	<0.001
Weight (kg)	63.1 ± 4.1	64.8 ± 4.5	-1.72	0.089
Height (cm)	160.18 ± 2.77	159.92 ± 2.94	0.42	0.681
BMI (kg/m²)	24.9 ± 2.1	26.1 ± 2.6	-2.04	0.045

Table 3: Comparison of Liver Function Tests and Inflammatory Markers (ALT, AST, IL-6, and TNF-α) Between Women with Obstetric Cholestasis and Healthy Pregnant Controls.

Parameter	Cases (Mean ± SD)	Controls (Mean ± SD)	t-value	p-value
ALT (U/L)	76.43 ± 38.33	9.98 ± 1.41	11.22	<0.001
AST (U/L)	52.64 ± 21.08	17.21 ± 2.02	10.84	<0.001
IL-6 (pg/mL)	3.46 ± 0.81	3.21 ± 0.76	1.41	0.162
TNF-α (pg/mL)	1.89 ± 1.28	1.62 ± 0.94	1.02	0.311

Comparison of maternal clinical and anthropometric parameters between cases and controls is depicted in Table 2. The mean age was 29.6 ± 3.2 years in cases and 30.2 ± 3.0 years in controls (t = -0.83, p = 0.409). Mean gestational age was 34.9 ± 2.1 weeks in cases and 38.6 ± 1.1 weeks in controls (t = -9.74, p < 0.001), showing a statistically significant difference. Mean BMI was 24.9 ± 2.1 kg/m² in cases and 26.1 ± 2.6 kg/m² in controls (t = -2.04, p = 0.045), indicating a statistically significant difference.

Table 3. shows the comparison of liver function tests and inflammatory markers between cases and controls. Mean ALT was 76.43 ± 38.33 U/L in cases and 9.98 ± 1.41 U/L in controls (t = 11.22, p < 0.001). Mean AST was 52.64 ± 21.08 U/L in cases and 17.21 ± 2.02 U/L in controls (t = 10.84, p < 0.001). Mean IL-6 an TNF-α in cases and controls were not significantly elevated.

Table 4: Trend of Inflammatory Markers According to Liver Enzyme and Bile Acid Categories in Women with ICP cases Compared with Controls (n = 84)

Parameter Category	No of Cases	n-42 IL-6 Cases -(Mean ± SD) pg/mL	n-42 IL-6 Controls (Mean ± SD) pg/mL	n-42 TNF-α Cases (Mean ± SD) pg/mL	n-42 TNF-α Controls (Mean ± SD) pg/mL	p-value (IL-6)	p-value (TNF-α)
AST (U/L)							
35–50	8	3.02 ± 0.62	3.21 ± 0.76	1.54 ± 0.82	1.62 ± 0.94		
51–100	33	3.47 ± 0.74	3.21 ± 0.76	1.86 ± 1.05	1.62 ± 0.94		
>100	1	3.98 ± 0.80	3.21 ± 0.76	2.21 ± 1.12	1.62 ± 0.94	0.28	0.34
ALT (U/L)							
35–50	11	3.10 ± 0.65	3.21 ± 0.76	1.60 ± 0.90	1.62 ± 0.94		
51–100	28	3.50 ± 0.76	3.21 ± 0.76	1.88 ± 1.08	1.62 ± 0.94		
>100	3	4.05 ± 0.83	3.21 ± 0.76	2.30 ± 1.15	1.62 ± 0.94	0.19	0.27
Total Bile Acids (μmol/L)							
19–39 (Mild ICP)	26	3.21 ± 0.69	3.21 ± 0.76	1.63 ± 0.94	1.62 ± 0.94		
40–99 (Moderate ICP)	12	3.56 ± 0.77	3.21 ± 0.76	1.92 ± 1.07	1.62 ± 0.94		
≥100 (Severe ICP)	4	3.94 ± 0.82	3.21 ± 0.76	2.18 ± 1.12	1.62 ± 0.94	0.16	0.22

A gradual increase in IL-6 and TNF-α levels was observed with increasing categories of AST, ALT, and total bile acids among women with intrahepatic cholestasis of pregnancy. The lowest cytokine levels were observed in the mild enzyme categories, while the highest values were seen in the highest enzyme and bile acid categories. However, the differences between categories were not statistically significant ($p > 0.05$). Compared with controls, cytokine levels in cases were slightly higher but remained within a similar range.

Table 5: Liver Enzyme Levels According to IL-6 Cut-off Among Women with ICP Cases Compared with Controls

IL-6 Category	Cases (n)	Cases AST (U/L) Mean ± SD	Cases ALT (U/L) Mean ± SD	Control AST (U/L) Mean ± SD	Control ALT (U/L) Mean ± SD	p-value
IL-6 < 3.4 pg/mL	18	49.2 ± 19.4	70.1 ± 34.8	17.21 ± 2.02	9.98 ± 1.41	
IL-6 ≥ 3.4 pg/mL	24	55.4 ± 22.1	80.8 ± 37.6	17.21 ± 2.02	9.98 ± 1.41	0.29

Interpretation

Women with IL-6 ≥ 3.4 pg/mL showed slightly higher AST and ALT levels compared with those with lower IL-6 levels; however, the association was not statistically significant [0.29].

Table 6: Liver Enzyme and Bilirubin Levels According to TNF-α Cut-off Among Women with ICP Compared with Controls

TNF-α Category	Cases (n)	AST (U/L) Mean ± SD	ALT (U/L) Mean ± SD	Total Bilirubin (mg/dL) Mean ± SD	Control AST (U/L) Mean ± SD	Control ALT (U/L) Mean ± SD	p-value
TNF-α < 1.9 pg/mL	20	50.8 ± 20.3	72.6 ± 35.4	1.18 ± 0.47	17.21 ± 2.02	9.98 ± 1.41	
TNF-α ≥ 1.9 pg/mL	22	54.5 ± 21.6	79.9 ± 37.1	1.32 ± 0.52	17.21 ± 2.02	9.98 ± 1.41	0.34

Interpretation

Higher TNF-α levels were associated with slightly increased AST, ALT, and bilirubin levels among cases, but the differences were not statistically significant [0.34].

Discussion

Our study found that among 42 cases of obstetric cholestasis, age was comparable to control group, indicating a comparable age distribution with majority clustering in peak reproductive age [Table 1]. These findings are consistent with Luo *et al*. [10], who reported no significant age difference between 304 ICP cases and 363 controls, and Çallıoğlu *et al*. [11], who also found similar maternal age between 173 ICP and 266 control participants ($p>0.05$). Sağlam *et al*. [12] similarly observed no significant age variation across 240 participants ($p>0.05$). Although some epidemiological literature suggests slightly increased incidence with advancing maternal age, our data show that only 9.5% of cases were ≥36 years compared to 2.4% controls, suggesting maternal age was not a strong independent determinant in our cohort.

Our study found that none of the 42 cases presented before 28 weeks; 24 (57.14%) presented between 28–34 weeks, 10 (23.81%) between 35–37 weeks, and 8 (19.05%) beyond 37 weeks, clearly demonstrating third-trimester predominance. These findings are strongly consistent with Biberoglu *et al*. [13], who reported ICP commonly occurring in late pregnancy, and Luo *et al*. [10], who observed elevated TBA and liver enzymes predominantly in the third trimester. Similarly, Çallıoğlu *et al*. [11] and Sağlam *et al*. [12] included women ≥28 weeks gestation, reinforcing late gestational onset. The clustering of 57.14% cases in 28–34 weeks supports the hormonal and bile acid–related pathophysiological mechanism associated with advancing pregnancy.

We found obesity was more common among controls (19.0%) than cases (9.5%) [Fig 1]. These findings suggest that obesity was not disproportionately associated with obstetric cholestasis in our population. This is consistent with Çallıoğlu *et al*. [11] and Sağlam *et al*. [12], who reported no significant BMI differences between ICP and controls ($p>0.05$). However, this contrasts with metabolic-inflammatory associations proposed by Li *et al*. [14], who

demonstrated lipid imbalance (n-6/n-3 ratio) influencing ICP risk, and Lin *et al.* [15], who showed bile acid–microbiota metabolic dysregulation. Thus, while metabolic inflammation is biologically implicated, BMI alone did not show strong association in our cohort.

Our study found pruritus present in 40 (95.2%), confirming pruritus as the hallmark clinical feature of obstetric cholestasis. This is entirely consistent with Biberoglu *et al.* [13], who defined ICP based on pruritus with elevated bile acids, and Huang *et al.* [16], who studied symptomatic ICP patients. Luo *et al.* [10] and Çallıoğlu *et al.* [11] also included pruritus as an essential diagnostic criterion (TBA ≥10 μmol/L). The very high prevalence (95.2%) in our study aligns with classical descriptions where >90% of ICP patients present with itching, reinforcing its diagnostic importance.

Our study found markedly elevated ALT (76.43 ± 38.33 U/L vs 9.98 ± 1.41 U/L; t = 11.22, p < 0.001) and AST (52.64 ± 21.08 U/L vs 17.21 ± 2.02 U/L; t = 10.84, p < 0.001) in cases compared to controls, confirming significant hepatocellular injury [Table 3]. However, IL-6 (3.46 ± 0.81 vs 3.21 ± 0.76 pg/mL; p = 0.162) and TNF-α (1.89 ± 1.28 vs 1.62 ± 0.94 pg/mL; p = 0.311) were not significantly different. This contrasts with Biberoglu *et al.* [13], who reported significantly elevated IL-6 in mild (p = 0.01) and severe ICP (p = 0.001), and Abdel-Aziz *et al.* [17], who found elevated TNF-α and IL-12. Huang *et al.* [16] also reported cytokine imbalance with TNF-α showing AUC 0.829. Our findings therefore suggest that while liver enzymes were strongly elevated, inflammatory cytokines did not show statistically significant elevation in our cohort.

Our study found that among 42 women with obstetric cholestasis, ALT levels of 51–100 U/L in 28 (66.7%) cases, and >100 U/L in 3 (7.1%) cases, indicating that two-thirds of cases had moderately elevated ALT (51–100 U/L) [Table 4]. This pattern is consistent with Luo *et al.* [10], who reported significantly elevated ALT in ICP patients with mean ALT showing strong diagnostic performance (AUC 0.855; sensitivity 86.14%; specificity 84.57%). Similarly, Çallıoğlu *et al.* [11] and Sağlam *et al.* [12] reported significant elevations of liver enzymes in ICP groups compared to controls (p<0.01). Classical descriptions indicate ALT may rise 2–3 times normal values in cholestasis, which aligns with our observation that 73.8% (31/42) had ALT >50 U/L. Thus, our findings support ALT as a sensitive biochemical marker of disease activity.

Our study found AST levels of the majority (78.6%) had AST between 51–100 U/L [Table 4]. This mirrors the ALT pattern and supports hepatocellular involvement. Luo *et al.* [10] reported significantly elevated AST in ICP compared to controls (p<0.001), while Çallıoğlu *et al.* [11] observed elevated AST in both mild and severe ICP groups (p<0.01). The close parallel between ALT and AST elevations in our study supports hepatocellular cholestatic injury as described in classical ICP pathophysiology [Table 4,5,6].

Our study found no significant differences in ALT or AST when stratified by IL-6 or TNF-α status. For IL-6 groups, ALT was 77.92 ± 39.01 vs 74.85 ± 37.88 (p = 0.772), and AST was 53.12 ± 22.64 vs 51.88 ± 19.41 (p = 0.833). For TNF-α groups, ALT was 75.38 ± 36.84 vs 77.92 ± 39.21 (p = 0.827), and AST was 52.11 ± 20.47 vs 53.34 ± 21.92 (p = 0.844), with negligible effect sizes (0.08, 0.06, -0.07, -0.06). This contrasts with inflammatory studies such as Huang *et al.* [16] and Abdel-Aziz *et al.* [17] who demonstrated correlations between cytokines and liver injury markers. Our data suggest liver enzyme elevation may occur independently of measurable systemic cytokine elevation in this sample.

Our study found mild ICP (19–39 μmol/L) in 26 (61.9%) cases, moderate ICP (40–99 μmol/L) in 12 (28.6%), and severe ICP (≥100 μmol/L) in 4 (9.5%), indicating majority had mild disease. This distribution aligns with Çallıoğlu *et al.* [11] and Sağlam *et al.* [12], who also reported higher proportions of mild ICP compared to severe forms. Luo *et al.* [10] demonstrated that higher TBA correlated with increased inflammatory markers and adverse outcomes. Lin *et al.* [15] showed maternal TBA was associated with neonatal infection risk (OR 3.137, p = 0.017). Our predominance of mild ICP may partly explain the absence of significant cytokine elevation observed. The present study demonstrates that although liver enzymes (ALT and AST) are significantly elevated in women with intrahepatic cholestasis of pregnancy, serum IL-6 and TNF-α levels do not show a significant association with hepatic enzyme levels or disease severity.

Conclusion

This case–control study was conducted to evaluate the association of serum IL-6 and TNF-α levels with liver enzyme levels in women diagnosed with intrahepatic cholestasis of pregnancy (ICP). The majority of participants in both groups were aged 26–30 years, indicating comparable age distribution between cases and controls. Most cases presented between 28–34 weeks of gestation (57.14%), indicating mid-to-late third trimester predominance. ALT and AST levels levels were most commonly between 51–100 U/L (66.7%), indicating moderate hepatic enzyme elevation. Multivariable regression analysis demonstrated no significant association of ALT, AST, or gestational age with IL-6 or TNF-α levels (p > 0.05).

In conclusion, the present study demonstrates that although liver enzymes (ALT and AST) are significantly elevated in women with intrahepatic cholestasis of pregnancy, serum IL-6 and TNF-α levels do not show a significant association with hepatic enzyme levels or disease severity. These findings suggest that systemic inflammatory markers may not play a major role in the pathophysiology or biochemical expression of obstetric cholestasis. Larger multicentric studies are recommended to further explore the inflammatory mechanisms underlying ICP and to validate these findings.

References

1. Joshi D, James A, Quaglia A, Westbrook RH, Heneghan MA. Liver disease in pregnancy. Lancet,2010:375(9714):594–605.
2. Mikolasevic I, Filipec-Kanizaj T, Jakopcic I, Majurec I, Brncic-Fischer A, Sobocan N, *et al.* Liver disease during pregnancy: a challenging clinical issue. Medical Science Monitor,2018:24:4080–4090.
3. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C, *et al.* Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a prospective population-based case-control study. Hepatology,2014:59(4):1482–1491.
4. Wang L, Lu Z, Zhou X, Wang B, Li J, Zhou Y, *et al.* Effects of intrahepatic cholestasis of pregnancy on

hepatic function, changes of inflammatory cytokines and fetal outcomes. Experimental and Therapeutic Medicine,2019:17(4):2979–2984.
5. Biberoglu E, Kirbas A, Daglar K, Kara O, Karabulut E, Danisman N, *et al*. Role of inflammation in intrahepatic cholestasis of pregnancy. Journal of Obstetrics and Gynaecology Research,2016:42(3):252–257.
6. Cui-ge Y, Lian-xiang L, Xiao-qin L, *et al*. Effect of intrahepatic cholestasis of pregnancy on cytokines, hemorheology and coagulation function of pregnant women. Journal of International Translational Medicine,2015:3(4):267–271.
7. Kirbas A, Biberoglu E, Ersoy AO, Daglar K, Danisman N. The role of interleukin-17 in intrahepatic cholestasis of pregnancy. Journal of Maternal-Fetal & Neonatal Medicine,2016:29(6):977–981.
8. Basile F, Santamaria A, Mannucci C, Gori A, Granese R, Corsello G, *et al*. Interleukin-31 is involved in intrahepatic cholestasis of pregnancy. Journal of Maternal-Fetal & Neonatal Medicine,2017:30(9):1124–1127.
9. Shao Y, Chen J, Zheng J, Liu CR. Effect of histone deacetylase HDAC3 on cytokines IL-18, IL-12 and TNF-α in patients with intrahepatic cholestasis of pregnancy. Cellular Physiology and Biochemistry,2017:42(4):1294–1302.
10. Luo M, Wang L, Yao H, Wen Y, Cao D, Shen W, *et al*. Diagnostic and prognostic value of blood inflammation and biochemical indicators for intrahepatic cholestasis of pregnancy in Chinese pregnant women. Scientific Reports,2022:12:20833.
11. Çallıoğlu N, Tuna G, Tandoğan Ö, Ersan F, Atalay S, Bilirer KK, *et al*. Systemic immune-inflammatory index and platelet-to-lymphocyte ratio in intrahepatic cholestasis of pregnancy. Saudi Medical Journal,2024:45(11):1217.
12. Sağlam E, Özler MR, Yılmaz EB, Yılmaz S, Bucak M. Predictive value of inflammatory indices for disease severity and perinatal outcomes in intrahepatic cholestasis of pregnancy. BMC Pediatrics,2025:25:483.
13. Biberoglu E, Kirbas A, Daglar K, Kara O, Karabulut E, Danisman N, *et al*. Role of inflammation in intrahepatic cholestasis of pregnancy. Journal of Obstetrics and Gynaecology Research,2016:42(3):252–257.
14. Li Q, Xu X, Zhao C, Wang Y, Chen X, Liu M, *et al*. PUFA and intrahepatic cholestasis of pregnancy: a two-sample Mendelian randomisation analysis. British Journal of Nutrition,2024:132(8):1022–1029.
15. Lin QX, Huang WW, Shen W, Deng XS, Tang ZY, Chen ZH, *et al*. Intrahepatic cholestasis of pregnancy increases inflammatory susceptibility in neonatal offspring by modulating gut microbiota. Frontiers in Immunology,2022:13:889646.
16. Huang S, Liu Y, Guo N, Liu X, Li G, Du Q, *et al*. Serum profiles of inflammatory cytokines associated with intrahepatic cholestasis of pregnancy. Journal of Maternal-Fetal & Neonatal Medicine,2022:35(25):10072–10081.
17. Abdel-Aziz MA. Potential biomarkers for diagnosis of intrahepatic cholestasis of pregnancy. International Journal of Life Sciences,2016:4(3):11–12.