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Original Research

Serum Taurocholic Acid Levels Have Predictive Value for Adverse Maternal and Infant Outcomes in Pregnant Women with Intrahepatic Cholestasis of Pregnancy: A Prospective Cohort Study

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Abstract

Background: Intrahepatic cholestasis of pregnancy (ICP) is a common liver disorder specific to pregnancy. Taurocholic acid (TCA) has been implicated in the pathogenesis of ICP. This study aimed to investigate the association between serum TCA levels and adverse maternal and infant outcomes in women with ICP. **Methods**: Pregnant women diagnosed with ICP were categorized into normal or adverse groups based on their pregnancy outcomes. Baseline data, including age, pre-pregnancy body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), and fasting blood sample (5 mL), were collected at 28 weeks of gestation. Serum levels of total bile acid (TBA), alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), and TCA were measured using a fully automatic biochemical analyzer. The predictive value of serum TCA levels for adverse outcomes in ICP was analyzed using receiver operating characteristic (ROC) curve analysis. Subsequently, ICP patients were divided into high and low TCA expression groups, and the changes in baseline data and adverse outcomes were compared between the groups. The relationship between serum TCA levels and adverse outcomes was evaluated using adverse maternal and infant outcome curves. Logistic regression analysis was performed to identify independent risk factors for adverse outcomes in ICP patients. **Results**: The adverse outcome group showed significant differences in gestational age at delivery (median value of 37 years old, $p = 0.0001$), levels of TBA (mean $\pm$ standard deviation 47.05 $\pm$ 6.43 µmol/L, $p < 0.0001$), ICP severity (proportion of severe ICP patients was 85.14%, $p < 0.0001$), ALT (mean $\pm$ standard deviation 82.59 $\pm$ 6.29 U/L, $p < 0.0001$), AST (median value of 67.50 U/L, $p < 0.0001$), and TBIL (mean $\pm$ standard deviation 47.05 $\pm$ 6.99 µmol/L, $p < 0.0001$), compared to the normal outcome group. Serum TCA levels were higher in the adverse outcome group (mean $\pm$ standard deviation 17.79 $\pm$ 4.56 µmol/L) than in the normal outcome group (mean $\pm$ standard deviation 11.72 $\pm$ 3.68 µmol/L) ($p < 0.001$). Serum taurocholic acid (TCA) levels demonstrated predictive value for adverse outcomes in ICP patients, and the areas under the ROC curve/sensitivity/specificity/cutoff value were 0.8430, 66.22%, 91.03%, and 16.17, respectively. The high TCA expression group had higher levels of TBA (median value of 43.40 µmol/L, $p < 0.0001$), ALT (median value of 79.89 µmol/L, $p < 0.0001$), AST (median value of 63.87 µmol/L, $p < 0.0001$), and TBIL (median value of 43.79 µmol/L, $p < 0.0001$), a higher proportion of severe ICP cases (71.43%, $p < 0.0001$). There were a remarkably increased number of adverse pregnancy outcomes (postpartum hemorrhage, premature birth, neonatal asphyxia, fetal distress, amniotic fluid fecal staining, and low birth weight) in the high TCA expression group (n = 49) compared to the low TCA expression group (n = 25) ($p < 0.0001$). The Kaplan-Meier (KM) curve of patients with high TCA expression shifted to the left compared with patients with low TCA expression ($p < 0.0001$). The cumulative survival rate of patients with high serum TCA expression (22.22%) was prominently reduced compared to patients with low serum TCA expression (85.03%), indicating that high serum TCA levels increased the risk of maternal and infant adverse outcomes in ICP patients. TBAs, AST, and TCA were identified as independent risk factors for adverse maternal and fetal outcomes in ICP patients. **Conclusion**: Serum TCA is an independent risk factor for adverse outcomes in ICP patients. Serum TCA levels have predictive values for adverse maternal and infant outcomes in pregnant women with ICP, but there are still some false positives. In clinical diagnosis, it is essential to combine other clinical data to increase the diagnostic accuracy.

Keywords: intrahepatic cholestasis of pregnancy; adverse maternal and infant outcomes; taurocholic acid; total bile acids; alanine transaminase; aspartate transaminase; total bilirubin

1. Introduction

During pregnancy, the body undergoes various anatomical and physiological changes to support the development of fetus [1]. One organ that adapts its metabolism during pregnancy is the liver, which plays a crucial role in transporting bile, and regulating bile acid levels in the blood [1]. While moderate increases in total bile acid (TBA) levels are normal, excessive elevation can lead to intrahepatic cholestasis of pregnancy (ICP) and increase the risk of adverse perinatal outcomes [2]. ICP is associated with adverse maternal and infant outcomes, including meconium staining of the amniotic fluid, spontaneous preterm delivery, and stillbirth [3–5]. The pathogenesis of ICP involves hormonal, genetic, environmental, and immunological factors, with the estrogen-bile acid axis playing a significant role [5]. However, the precise etiology of ICP remains poorly understood, and its management remains challenging due to limited data on diagnosis, treatment, and associated adverse outcomes [6]. Early diagnosis and timely management of ICP can significantly reduce the risk of complications, including unexpected intrauterine death [3]. Therefore, there is an urgent need to identify reliable biomarkers for ICP.

In ICP, taurochenodeoxycholic acid (TCDCA), glycocholic acid (GA), tauroursodeoxycholic acid (TUDCA), taurocholic acid (TCA), and glycochenodeoxycholic acid (GDA) are the predominantly affected bile acids [7]. Previous studies have reported a correlation between elevated serum TCA levels and the severity and clinical prognosis of drug-induced liver injury [8]. Among the bile acids, TCA and GA are the most prominent types detected in the serum of severe ICP patients, with levels significantly higher than those in mild ICP or normal pregnant women, among which TCA has been identified as a promising biomarker for predicting the risk of fetal complications [9]. However, research on TCA in the context of ICP patients remains limited, with most studies focusing on overall bile acid metabolism [7]. Therefore, this study aimed to investigate the serum levels of TCA in pregnant women with ICP and explore the relationship between TCA levels and adverse maternal and infant outcomes, with the goal of improving perinatal outcomes.

2. Materials and Methods

2.1 Ethics Statement

The present study was reviewed and approved by the Academic Ethics Committee of the Third Affiliated Hospital of Zhengzhou University, and conducted in accordance with the principles outlined in the Declaration of Helsinki (approval number: 2023-168-01). Informed consent was obtained from all participants after providing a detailed explanation of the study objectives and procedures.

2.2 Study Subjects

This prospective analysis included a total of 372 pregnant women diagnosed with ICP who were admitted to the Third Affiliated Hospital of Zhengzhou University between January 2020 and December 2022 due to skin itching. Among them, 85 patients did not meet the inclusion criteria, 36 refused to participate, 11 withdrew from the study, and 10 had incomplete data. Ultimately, 230 pregnant women with ICP were included in the study. Based on their maternal and infant outcomes, the participants were allocated to two groups: the normal group (with good perinatal outcomes, n = 156) and the adverse group (with poor perinatal outcomes, n = 74). Mild ICP was defined as TBA levels ranging from 10 to 40 μmol/L, while severe ICP was defined as TBA $\geq$40 μmol/L [10]. The pregnancy outcomes of all ICP patients were documented, and good maternal and infant outcomes were defined as normal deliveries with healthy newborns. Maternal and infant adverse outcomes included postpartum hemorrhage, premature delivery (<37 weeks), neonatal asphyxia, fetal distress, amniotic fluid fecal contamination, and low birth weight (<2500 g). The research flowchart is depicted in Fig. 1.

2.3 Inclusion Criteria

The following inclusion criteria were applied: (1) diagnosed with ICP based on elevated serum TBA levels (TBA >10 μm/L) or/and increased transaminase levels, with skin itching as the main clinical symptom, and no other diseases that could produce similar laboratory test results and symptoms [10]; (2) singleton pregnancy; (3) primiparous women; (4) conception by spontaneous ovulation; (5) availability of complete clinical data.

2.4 Exclusion Criteria

The following exclusion criteria were applied: (1) twin or multiple pregnancies; (2) multiparous women; (3) history of hepatobiliary system diseases; (4) use of hormone drugs to induce ovulation or assisted reproductive technologies; (5) deranged liver function tests (LFT) with low TBA; (6) skin itching caused by other etiologies; (7) presence of pregnancy complications such as gestational diabetes mellitus, hypertension, and anemia; (8) concurrent dysfunction of organs such as heart or kidneys; (9) missing diagnostic records; (10) unclear ICP diagnosis.

2.5 Data and Sample Collection

Baseline data of pregnant women with ICP were collected at 28 weeks of gestation, including age, pre-pregnancy body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), and a 5 mL fasting blood sample obtained from the elbow vein. The gestational age at the time of delivery in ICP was also recorded. The fasting blood sample from the elbow vein was centrifuged at 2000 r/min for 20 minutes, and the upper serum was collected in sterile Eppendorf tubes and stored at –80

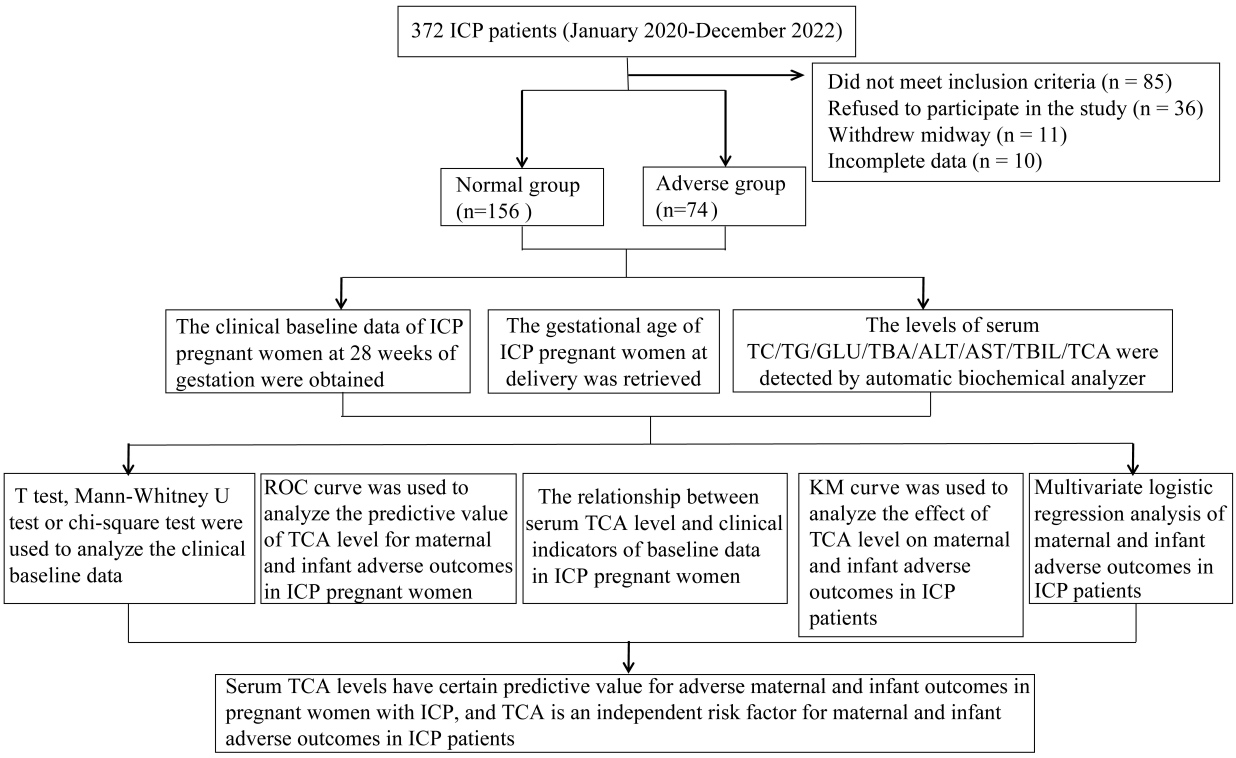

Fig. 1. Research on the relationship between serum TCA levels and adverse maternal and infant outcomes in pregnant women with ICP. ICP, intrahepatic cholestasis of pregnancy; n, number; TC, total cholesterol; TG, triglyceride; GLU, fasting blood glucose; TBA, total bile acid; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin; TCA, taurocholic acid; ROC, receiver operating characteristic; KM, Kaplan-Meier.

°C. The levels of serum total cholesterol (TC), triglyceride (TG), fasting blood glucose (GLU), TBA, alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin (TBIL), and TCA were measured using an automatic biochemical analyzer (Perlong Technology, Beijing, China). TC, TG, TBA, ALT, AST, TBIL, and TCA kits were all purchased from Biolab Technology (Beijing, China), and the GLU kit was obtained from Maccura Biotechnology (Chengdu, Sichuan, China). The biochemical analyzer was calibrated at regular intervals to ensure the accuracy of biochemical test results.

2.6 Data Analyses

The sample size was estimated using G-Power version 3.1.9.2 (Franz Faul, Kiel, Germany). The sample size of the independent sample *t*-test for each group was determined to be at least 64, and the total sample size was set to be at least 128. For the Chi-square test, the total sample size was determined to be at least 220 (**Supplementary Fig. 1**). Data analyses and plotting were performed using the GraphPad Prism 6.0 software (GraphPad Software, San Diego, CA, USA). The Shapiro-Wilk test was used to assess the normal distribution of data. Normally distributed measurement data were presented as mean ± standard deviation and analyzed using the independent sample *t*-test. Non-normally distributed measurement data were presented as quartiles and analyzed using the Mann-Whitney U test. Counting data were presented as the number of cases and analyzed using the Chi-square test. The predictive value of TCA for adverse perinatal outcomes in pregnant women with ICP was evaluated using receiver operating characteristic (ROC) curve. Kaplan-Meier (KM) curves were generated to analyze the impact of serum TCA levels on adverse maternal and fetal outcomes in ICP patients. Statistical significance was set at $p < 0.05$.

3. Results

3.1 Clinical Baseline Characteristics

A total of 230 pregnant women with (ICP were included in this study, with 156 assigned to the normal group, and 74 to the adverse group, based on pregnancy outcomes. Statistical analyses of clinical baseline characteristics (Table 1) revealed no significant differences between the normal group and the adverse group in terms of age, pre-pregnancy BMI, blood pressure (SBP, DBP), blood lipids (TC, TG), and GLU ($p > 0.05$). However, significant differences were observed in gestational age at delivery, TBA levels, severity of ICP, ALT, AST, and TBIL levels (all $p < 0.05$).

Table 1. Clinical baseline data of the enrolled subjects.

Feature	Normal group (n = 156)	Adverse group (n = 74)	*p*-value
Age (years)	29 (23, 35)	29 (23, 34)	0.239
Pre-pregnancy BMI (kg/m^2)	22.47 (20.23, 23.96)	22.26 (19.94, 23.85)	0.142
Gestational age at delivery (weeks)	38 (37, 40)	37 (35, 39)	0.0001
SBP (mmHg)	116.60 ± 10.47	118.80 ± 10.84	0.1342
DBP (mmHg)	75.00 (60.00, 89.00)	76.50 (61.00, 89.00)	0.3183
TC (mmol/L)	5.89 ± 0.81	5.85 ± 0.98	0.7633
TG (mmol/L)	3.37 ± 0.71	3.48 ± 0.69	0.2234
GLU (mmol/L)	4.72 ± 0.61	4.78 ± 0.71	0.5366
TBA (µmol/L)	32.75 ± 5.56	47.05 ± 6.43	<0.0001
ICP disease severity			
Mild ICP (10–40 µmol/L), %	141 (90.38%)	11 (14.86%)	<0.0001
Severe ICP (≥40 µmol/L), %	15 (9.62%)	63 (85.14%)	
ALT (U/L)	71.35 ± 3.45	82.59 ± 6.29	<0.0001
AST (U/L)	52.33 (41.37, 60.14)	67.50 (40.73, 77.82)	<0.0001
TBIL (µmol/L)	32.70 ± 4.21	47.05 ± 6.99	<0.0001

Note: BMI, body mass index; n, number; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; GLU, fasting blood glucose; TBA, total bile acid; ICP, intrahepatic cholestasis of pregnancy; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin. Data conforming to normal distribution were depicted as mean ± standard deviation. The data of SBP, TC, TG, GLU, TBA, ALT, and TBIL between two groups were subjected to independent sample *t*-test. Non-normal distribution data were expressed as median (minimum, maximum) values. Age, pre-pregnancy BMI, gestational age at delivery, DBP, and AST were subjected to Mann-Whitney U test. The counting data were expressed in terms of number of cases and percentages, and tested by Chi-square test.

3.2 Differential Expression Levels of Serum TCA in ICP Pregnant Women

The serum TCA levels of ICP pregnant women were measured in the normal group (11.72 ± 3.68 µmol/L) and the adverse group (17.79 ± 4.56 µmol/L), and it was found that TCA levels were significantly higher in the adverse group ($p < 0.001$) (Fig. 2).

3.3 Predictive Value of Serum TCA Levels for Adverse Maternal and Fetal Outcomes in ICP Pregnant Women

ROC curves were generated to assess the predictive value of serum TCA levels for adverse maternal and fetal outcomes in ICP pregnant women. The area under the curve (AUC) for serum TCA levels predicting adverse perinatal outcomes in ICP pregnant women was 0.8430. The optimal cut-off value was determined to be 16.17, with a sensitivity of 66.22%, and specificity of 91.03% (Fig. 3). These findings indicate that TCA has predictive value for adverse maternal and infant outcomes in ICP pregnant women.

3.4 Relationship between Serum TCA Levels and Baseline Data in ICP Pregnant Women

Based on the ROC cut-off value of TCA (16.17), the ICP pregnant women were divided into the low TCA expression group (n = 167) and the high TCA expression group (n = 63). The changes in baseline data were compared and analyzed. There were no significant differences between the two groups in terms of age, pre-pregnancy BMI, blood pressure (SBP, DBP), blood lipids (TC, TG), and GLU ($p > 0.05$). However, the high TCA expression group had a significantly lower gestational age at delivery, and higher levels of TBA, ALT, AST, and TBIL, compared to the low TCA expression group. The proportion of severe ICP was also higher in the high TCA expression group (all $p < 0.0001$) (Table 2).

3.5 Impact of Highly-Expressed Serum TCA on Adverse Maternal and Fetal Outcomes in ICP Pregnant Women

The relationship between serum TCA levels in ICP pregnant women and adverse pregnancy outcomes was further examined by grouping the patients into high and low TCA expression groups. The high TCA expression group had a significantly higher number of adverse maternal and fetal outcomes (postpartum hemorrhage, premature delivery, neonatal asphyxia, fetal distress, amniotic fluid fecal staining, low birth weight) compared to the low TCA expression group ($p < 0.0001$) (Table 3). KM curve and Log-rank test revealed that the KM curve of patients with high serum TCA expression levels shifted to the left compared to those with low TCA expression levels ($p < 0.0001$) (Fig. 4). The cumulative survival rate was substantially lower in the high TCA expression group compared to the low TCA expression (22.22% *vs*. 85.03%) ($p < 0.0001$). These findings indicate an increased risk of adverse maternal and fetal outcomes in ICP pregnant women with high serum TCA levels.

Table 2. The relationship between serum TCA levels and baseline clinical indicators in ICP pregnant women.

Feature	Low TCA (n = 167)	High TCA (n = 63)	*p*-value
Age (years)	29 (23, 35)	29 (23, 34)	0.1145
Pre-pregnancy BMI	22.42 (20.10, 23.94)	22.22 (19.94, 23.96)	0.2081
Gestational age at delivery (weeks)	38 (35, 40)	37 (35, 40)	0.0010
SBP (mmHg)	116 (94.00, 140.00)	119.0 (92.00, 137.00)	0.1858
DBP (mmHg)	76.00 (60.00, 89.00)	76.00 (62.00, 89.00)	0.3159
TC (mmol/L)	5.91 ± 0.78	5.79 ± 1.07	0.3745
TG (mmol/L)	3.38 ± 0.71	3.48 ± 0.70	0.3284
GLU (mmol/L)	4.71 ± 0.63	4.83 ± 0.68	0.2035
TBA (μmol/L)	35.01 (17.72, 59.54)	43.40 (27.55, 58.95)	<0.0001
ICP disease severity			
Mild ICP (10–40 μmol/L), %	134 (80.24%)	18 (28.57%)	<0.0001
Severe ICP (≥40 μmol/L), %	33 (19.76%)	45 (71.43%)	
ALT (U/L)	73.11 (61.72, 94.63)	79.89 (65.64, 93.88)	<0.0001
AST (U/L)	54.39 (40.73, 74.66)	63.87 (46.01, 77.82)	<0.0001
TBIL (μmol/L)	34.87 (20.71, 59.54)	43.79 (26.41, 58.95)	<0.0001

Note: BMI, body mass index; n, number; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglyceride; GLU, fasting blood glucose; TBA, total bile acid; ALT, alanine transaminase; AST, aspartate transaminase; TBIL, total bilirubin. Data conforming to normal distribution were depicted as mean ± standard deviation. The data of TC, TG, and GLU between two groups were subjected to independent sample *t*-test. Non-normal distribution data were expressed as median (minimum, maximum) values. Age, pre-pregnancy BMI, gestational age at delivery, SBP, DBP, TBA, ALT, AST, and TBIL were subjected to Mann-Whitney U test. The counting data were expressed in terms of number of cases and percentages, and tested by Chi-square test.

Table 3. Comparisons of adverse pregnancy outcomes between low and high TCA expression groups in ICP pregnant women.

Feature	Low TCA (n = 167)	High TCA (n = 63)	*p*-value
Postpartum hemorrhage	4	9	
Premature delivery	9	13	
Neonatal asphyxia	2	6	
Fetal distress	4	8	
Amniotic fluid fecal staining	4	8	
Low birth weight	8	11	
Total number of adverse outcomes	31	55	<0.0001

Note: The number was expressed as n, and the comparisons were conducted using the Chi-square test.

3.6 Multivariate Logistic Regression Analyses of Adverse Perinatal Outcomes in ICP Patients

Multivariate logistic regression analyses were conducted to identify independent risk factors for adverse maternal and fetal outcomes in ICP patients. Gestational age at delivery, TBA, ICP severity, ALT, AST and TBIL, which showed significant differences with $p < 0.05$ in the clinical baseline characteristics (Table 1), as well as TCA, were included as independent variables. The results showed that TBA, ALT, and TCA were independent risk factors for adverse maternal and fetal outcomes in ICP patients (all $p < 0.05$) (Table 4).

Table 4. Multivariate logistic regression analyses of adverse maternal and infant outcomes in ICP patients.

Variable	OR	95% CI	*p*-value
Gestational age at delivery	0.942	0.270–3.288	0.925
TBA	1.660	1.022–2.697	0.041
ICP severity	7.775	0.074–815.700	0.388
ALT	1.384	1.002–1.912	0.049
AST	1.233	0.990–1.535	0.061
TBIL	1.036	0.789–1.360	0.801
TCA	1.422	1.021–1.979	0.037

OR, odds ratio; 95% CI, 95% confidence interval.

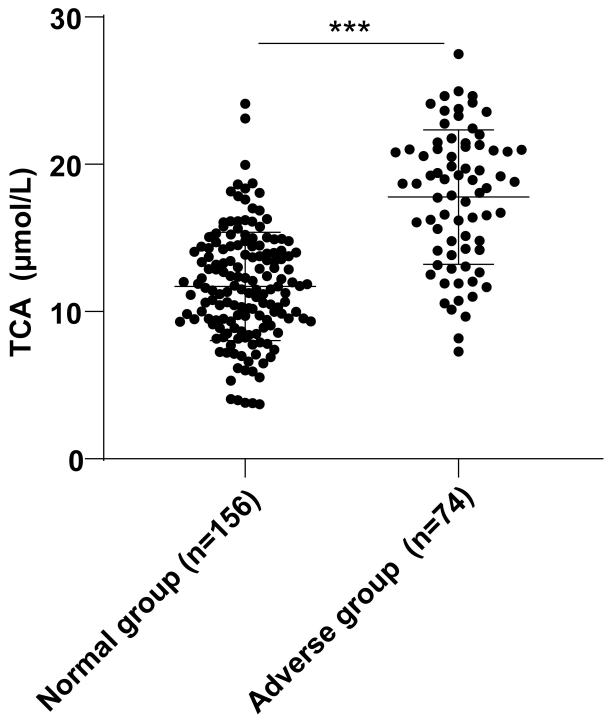

Fig. 2. Differential expression levels of serum TCA in ICP pregnant women. Data conforming to normal distribution were expressed as mean ± standard deviation, and comparisons between two groups were conducted using independent sample *t*-test. n, number; ***, $p < 0.001$.

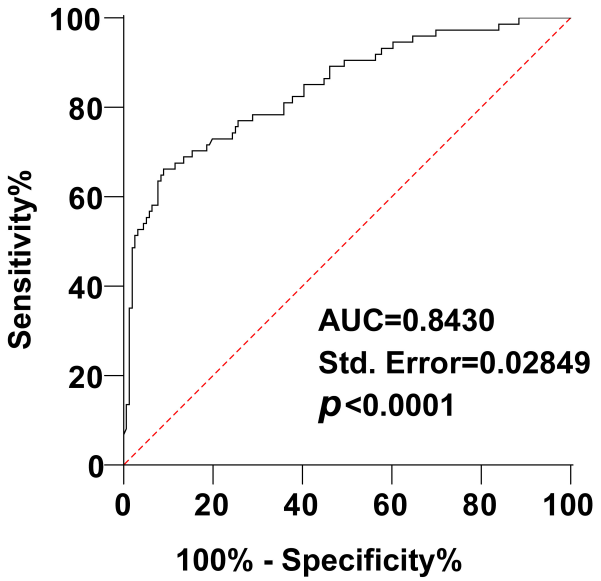

Fig. 3. The predictive value of TCA levels for adverse maternal and infant outcomes in ICP pregnant women was analyzed using the ROC curve. AUC, area under the curve.

4. Discussion

ICP is a common liver disorder that occurs during pregnancy and can have adverse effects on both the mother and the fetus [6]. While the prognosis for mothers with ICP is generally favorable, they often experience intense pruritus, which significantly impacts their quality of life [6]. On the other hand, the fetus is at increased risk of adverse outcomes, including stillbirth, spontaneous preterm birth, and meconium staining of the amniotic fluid [4,5,11]. Therefore, it is crucial to identify biomarkers that can predict adverse perinatal outcomes in ICP patients, as this can aid in fetal surveillance and treatment to prevent and reduce the occurrence of such outcomes. ICP is a liver disorder that only happens during pregnancy [12]. The changes in enzyme activity in liver cells during liver disease are reflected in the changes in enzyme activity in the serum [13]. For instance, alcohol dehydrogenase (ADH) and acetaldehyde dehydrogenase in serum are indicators of hepatocyte injury [14]. ADH has been proposed as a marker for the diagnosis of ICP in pregnant women [12]. Currently, there are a few highly specific biomarkers for ICP that are undetectable in healthy individuals, but can be detected in small amounts in the early stages of the disease. Previous studies have suggested the potential role of postprandial bile acids in predicting perinatal outcomes in ICP, with primary bile acid species, especially glycocholic acid (GA) and TCA, being prominently elevated in severe ICP patients [15]. Therefore, we hypothesized that TCA, as a crucial bile acid, might serve as a predictive factor for adverse maternal and infant outcomes. In this study, we aimed to investigate the relationship between serum TCA levels and adverse outcomes in pregnant women with ICP. Our results demonstrated that serum TCA levels had predictive value for adverse outcomes in pregnant women with ICP. However, further research is necessary to validate these findings and establish the clinical utility of TCA as a predictive biomarker.

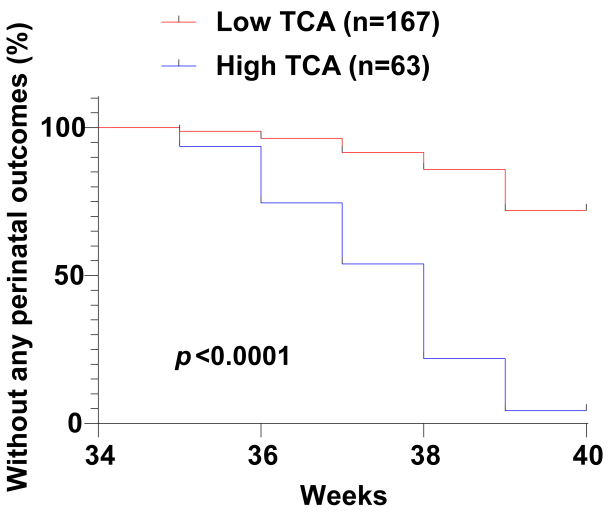

Fig. 4. Kaplan-Meier curve analyses of the impact of serum TCA levels on adverse maternal and fetal outcomes in ICP patients.

Pruritus and a decrease in LFT are common clinical manifestations of ICP, along with elevated levels of TBA [16]. Elevated concentrations of serum bile acid have been associated with an increased risk of preterm birth and stillbirth, particularly in singleton pregnancies and ICP patients with serum bile concentrations of 100 µmol/L or higher [17]. Monitoring prenatal indexes such as AST, ALT, TBA, and TBIL levels in pregnant women with ICP is crucial for predicting perinatal prognosis [18]. Consistent with previous findings, our study revealed significant differences in gestational age at delivery, TBIL, AST, ALT, and TBA levels, and ICP severity between the normal and adverse groups. These results highlight the importance of these parameters in assessing the prognosis of ICP and predicting adverse outcomes.

TCA has been shown to have significant effects on fetoplacental arterial pressures in a dual perfusion placental cotyledon model, suggesting its potential role in ICP [19]. Consistent with previous studies, our results revealed elevated serum levels of TCA in ICP patients with adverse perinatal outcomes. Severe ICP patients have been reported to exhibit higher serum levels of TCA, TCDCA, TUDCA, GA, and GDA normal pregnancy or mild ICP [9]. To further evaluate the predictive value of serum TCA levels for adverse perinatal outcomes in ICP pregnant women, we conducted ROC curves analyses, which yielded an AUC of 0.8430, with 66.22% sensitivity and 91.03% specificity. The results indicated that the sensitivity of serum TCA levels to predict maternal and infant adverse outcomes in ICP pregnant women was low (<70%), and the sensitivity referred to the "true-positive rate" [20], which suggested there was an excessively high false-positive rate. Hence, it may be necessary to expand the sample size to further verify the predictive value of serum TCA levels for adverse outcomes in ICP pregnant women, and the incorporation of other clinical data in the clinical diagnosis is required to enhance the diagnostic accuracy. These findings are in line with a previous study that identified total primary bile acids, including TCA, as the best biomarker for ICP, with the lowest false-negative and false-positive rates [9].

Furthermore, we classified ICP patients into low and high TCA level groups, and observed that those with high TCA levels had significantly decreased gestational age at delivery, elevated ALT, TBA, TBIL and AST levels, a higher proportion of severe ICP, a greater number of adverse perinatal outcomes (including premature delivery, postpartum hemorrhage, fetal distress, neonatal asphyxia, low birth weight, and amniotic fluid fecal staining), and an increased risk of developing perinatal outcomes. Consistent with our findings, previous studies have reported higher TCA levels in pregnant women with more severe ICP, which were associated with increased incidence of preterm birth and reduced gestational age at delivery [21,22]. Additionally, we identified TBA, TCA, and ALT as independent risk factors for adverse maternal and infant outcomes in ICP patients. Similar studies have shown that elevated ALT levels and the presence of meconium-stained amniotic fluid, delivery before 34 weeks of gestation, and composite adverse perinatal outcomes are more common in severe ICP cases compared to mild cases [23]. In twin pregnancies complicated by ICP, TBA >40 µmol/L has been associated with composite adverse outcomes, highlighting the need for enhanced treatment and fetal surveillance in ICP patients with these characteristics [23].

5. Conclusion

In summary, our study provides evidence supporting the high predictive value of serum TCA levels for adverse perinatal outcomes in pregnant women with ICP. TCA also serves as an independent risk factor for adverse outcomes in ICP patients. However, there are limitations to our research. Lipid profiling is a targeted metabolomics platform that can comprehensively analyze lipid types. Mass spectrometry can provide molecular weight information by measuring the mass-to-charge ratio (m/z) of the ionized substance. Many modern mass spectrometers can achieve mass accuracy of 0.001–0.002 m/z, which makes the lipid profile of compounds similar to m/z searches through databases or identification of ionized molecules via various commercial or open-sourced software. We did not conduct lipid profiling experiments due to limited resources and funding. In our study, serum TC, TG, and GLU were assessed using an automatic biochemical analyzer. Besides, the sample size of this study is relatively small, and we will further expand the sample size for in-depth research in the future.

Availability of Data and Materials

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Author Contributions

Guarantor of integrity of the entire study, study concepts, study design: YC, HL, HG; definition of intellectual content, literature research, clinical studies, experimental studies: YC, HL; data acquisition, data analysis: HG; statistical analysis: YC, JZ; manuscript preparation, manuscript editing, manuscript review: YC, JZ. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The present study was reviewed and approved by the Academic Ethics Committee of the Third Affiliated Hospital of Zhengzhou University, and conducted in accordance with the principles outlined in the Declaration of Helsinki (approval number: 2023-168-01). Informed consent was obtained from all participants after providing a detailed explanation of the study objectives and procedures.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/j.ceog5012257.

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