

Maternal and Fetal Outcomes of Patients with Liver Cirrhosis: A Case-Control Study

Xiang Gao

Beijing Youan Hospital, Capital Medical University

Yunxia Zhu

Beijing Youan Hospital, Capital Medical University

Haixia Liu

Beijing Youan Hospital, Capital Medical University

Hongwei Yu

Beijing Youan Hospital, Capital Medical University

Ming Wang (✉ 18763431543@163.com)

Capital Medical University <https://orcid.org/0000-0002-4628-8826>

Research article

Keywords: liver cirrhosis, pregnancy, CTP score, HBV

Posted Date: August 18th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-56781/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at BMC Pregnancy and Childbirth on April 8th, 2021. See the published version at <https://doi.org/10.1186/s12884-021-03756-y>.

Abstract

Objective:

We aimed to describe the characteristics and outcomes in pregnant women with liver cirrhosis, and identify the predictors of negative outcome of the mother and fetus.

Methods:

Retrospectively collect the mothers with liver cirrhosis in our center from 6/2010 to 6/2019. Women without liver cirrhosis were selected as a control in a 1:2 ratio. The primary assessment was the frequency of negative maternal and fetal outcomes. The secondary assessment was the negative outcomes between patients continuing the pregnancy or not and the factors to predict the severe negative outcomes.

Results:

Of 126 pregnancies enrolled, 29 pregnancies were discontinued for worrying the disease progression and 97 pregnancies were continued. 194 pregnancies without liver cirrhosis were selected as control. At baseline, patients with liver cirrhosis have a lower level of platelet, hemoglobin, Prothrombin activity, and a higher level of ALT, Total Bilirubin, Creatinine. Compared to control, patients with liver cirrhosis have a higher frequency of negative outcomes, including bleeding gums(7.2 %vs. 1.0%), TBA elevation (18.6 %vs.3.1%), infection (10.3 %vs.0.5%), cesarean section (73.6 %vs.49.5%), postpartum hemorrhage(13.8% vs 2.1%), blood transfusion (28.9% vs 2.1%), new ascites or aggravating ascites(6.2% vs.0%), MODS(7.2% vs.0.5%) and intensive care unit admissions(24.1% vs 1.1%). The incidence of severe maternal negative outcomes was also higher (32.0% vs 1.5%). Women who chose to discontinue the pregnancy had less severe negative outcomes (3.4% vs.32.0%).

A higher frequency of fetal/infants complication were observed in liver cirrhosis population than control, including newborn asphyxia(10.2% vs1.1%), Low birth weight infant(13.6% vs. 2.6%) .In those patients who progressed into the third trimester, multivariable regression demonstrated that severe negative outcomes were associated with a higher CTP scores (OR 2.128, 95% CI[1.002, 4.521] ,p=0.049). Wilson's disease related liver cirrhosis has a better prognosis (OR= 0.009, 95% CI[0, 0.763], p=0.038).

Conclusions:

The incidence of the negative outcomes was significantly increased in pregnancies complicated by cirrhosis. The predictor of severe negative outcomes is higher CTP score and Wilson's disease induced liver cirrhosis have a better prognosis. Timely terminate the pregnancy during the first trimester may avoid the incidence of severe negative outcomes.

Introduction

Liver cirrhosis is a chronic hepatocyte injury with extensive fibrosis and nodular regeneration¹. Pregnancy with liver cirrhosis is uncommon due to disturbances in endocrine metabolism, especially estrogen²⁻³. With improved therapeutic options for liver disease, more women are presenting for prenatal care with concomitant cirrhosis⁴.

Pregnant women with advanced cirrhosis are associated with an increased risk of complications

such as new-onset or deteriorated ascites for blood volume changes, bleeding from esophageal varices, liver failure, and hepatorenal syndrome⁵⁻⁶. Besides the deteriorate complication of liver cirrhosis, negative outcomes of mothers and fetuses, such as spontaneous abortion, stillbirth, fetal or neonatal demise, placental abruption, preeclampsia, preterm delivery, small-for-gestational-age neonate, and postpartum hemorrhage are at an increased risk in women with cirrhosis⁷.

Limited data exists regarding the negative maternal and fetal outcomes in mothers with liver cirrhosis. The majority of studies are case series^{3,7-9} and further studies involving larger patient populations are necessary to better guide clinical decision-making, improve prognosis, allow risk stratification, and design clinical trials. Therefore, we conducted a comparative study about the negative maternal outcomes (liver-related adverse events and obstetrical complications) and fetal/infant outcomes. Also, we evaluate the predictors and potential measures to improve the outcomes of the mother and fetus by comparing cirrhosis mothers with and those without negative outcomes.

Materials And Methods

Patient Selection and study design

Retrospective analysis of case records was carried out between June 2010 and June 2019 in the departments of the Beijing YouAn Hospital in China, a tertiary care hospital for liver diseases, including pregnant women diagnosed to have liver cirrhosis during pregnancy. The relevant institutional ethics review committee approved the trial (approval number: Jing-you-ke-lun-zi (2020)050) and the need for informed consent was obtained.

Patients at our clinic and in-patient services were screened for the following eligibility criteria: age between 20 and 45 years; clinical diagnosed as liver cirrhosis (Fibroscan or serum marker, or liver biopsy before showed stage IV fibrosis, or clinical signs of cirrhotic complications including but not limited to varices, ascites, encephalopathy, hepatorenal syndrome, by CPT score B or C), before or during the pregnancy; delivered in Beijing YouAn hospital institution where both gastrointestinal and prenatal follow-up visits were conducted. A group of pregnant mothers without liver cirrhosis were randomly selected in a 1:2 ratio to serve as the control group. Key exclusion criteria: liver diseases without cirrhosis caused by other reasons including Wilson disease, activated hepatitis B or C, hemophagocytic lymphohistiocytosis, hepatocellular carcinoma, or cytotoxic drugs.

Study Procedures and Data Collections

Using an electronic medical record system and paper charts, the following data from the clinic and inpatient services at YouAn Hospital were collected for analysis: baseline information at first trimester including age, gravidity, parity, Lab of the first visit including platelet, hemoglobin, alanine transaminase(ALT), albumin, total bilirubin, prothrombin activity, and creatinine, pertinent physical findings. For women with liver cirrhosis, additional data collection was performed that included documentation of gestational weeks at the time of the diagnosis and clinical signs.

Outcome Measurements

Our primary outcomes were the frequency of negative maternal outcomes (maternal complications and mortality) and fetal/infant outcomes. Negative maternal outcomes including pregnancy complications, obstetrical complications, liver-related complications (including ALT elevation (>2ULN), liver failure, deteriorate of symptoms of liver cirrhosis, renal failure, coagulation disorders, shock, and Infection). The aforementioned outcomes will be compared between groups. Pregnancy complication and obstetric complications including hypothyroidism during pregnancy, pregnancy-induced hypertension (PIH), gestational diabetes (GDM), placenta previa, data regarding medications, pregnancy complications, postpartum hemorrhage (>1000ml in cesarean section, >500ml in vaginal delivery, >400ml in abortion) and other obstetric complications were also collected during the delivery or after the delivery.

Our secondary outcomes were to evaluate the risk of deteriorating symptoms of liver cirrhosis between continuing and discontinuing pregnancy. Also, the role of predelivery splenectomy and intrauterine balloon in reducing postpartum hemorrhage, hysterectomy, and severe negative maternal outcomes. Severe negative outcomes include placenta abruption, postpartum hemorrhage(>1000ml), hysterectomy, poor wound healing, infection, MODS, subarachnoid hemorrhage, coagulation disorders, new ascites or aggravating ascites, upper gastrointestinal hemorrhage, fetal death, ALT elevation(>10ULN).

Statistical Analysis

Baseline characteristics and laboratory results were summarized for two groups utilizing descriptive statistics, including percentage, means \pm standard deviation (SD), and 95% CI. For the quantitative variable, the t-test was used to compare group differences. For categorical variables, the chi-square test was used for group comparisons. Multivariate classification logistic regression was used to adjust variables on predicting negative outcomes. Negative outcomes were replaced with 1 and normal outcomes were replaced with 0 during regression. The significance level was set at $P < 0.05$, all data were analyzed by SPSS 23.0 (SPSS, IBM., New York).

Results

Study Population

During the enrollment period, the consecutive medical records of 1708 pregnancies at our center were reviewed. Among them, 1582 pregnancies were excluded for not progressed into liver cirrhosis (**Fig. 1**)

and 126 pregnancies were diagnosed with liver cirrhosis before or during pregnancy. **97** pregnancies continued the pregnancy were enrolled into group A and **29** pregnancies discontinued for the concerning of disease progression were enrolled into group B. The group A were matched with 194 patients (1:2 ratio) without liver diseases based on the registration numbers and assigned to group C. All patients who received cesarean section in group A were further assigned into group A1 if the intrauterine balloon was used to prevent the postpartum hemorrhage or group A2 if not. The patients who were screened and enrolled in the different study groups are shown in **Fig 1**.

The Outcomes of the patients with liver cirrhosis or not

The clinical characteristics of patients at screening in each group are shown in **Table 1**. When compared to patients without liver cirrhosis (**group C**), patients with liver cirrhosis have significantly lower level of platelet(123.51 ± 66.66 vs. $239.60 \pm 54.70 \times 10^9/L$, $P=4.34 \times 10^{-40}$), hemoglobin(117.37 ± 14.91 vs. 124.97 ± 14.13 g/L, $P=3.7 \times 10^{-7}$), Prothrombin activity (96.79 ± 17.27 vs. $105.87 \pm 11.14\%$, $p=1.0 \times 10^{-5}$) and higher level of ALT(43.38 ± 60.49 vs. 20.74 ± 21.42 IU/L, $p=5.98 \times 10^{-4}$), Total Bilirubin(20.35 ± 39.31 vs. 11.00 ± 6.78 umol/L, $p=0.023$), and Creatinine (45.72 ± 7.49 vs. 43.00 ± 6.65 umol/L, $p=2.25 \times 10^{-3}$). There were no differences of the other baseline values between two groups, including the age (30.79 ± 5.01 vs. 31.38 ± 4.13 , $p=0.322$), ratio of primigravida (36.1% vs. 40.2%), and **multiple** pregnancy times (33% vs. 48.2%).

As shown in table 2, a significantly higher frequency of negative outcomes (71.1% [69/97] vs 12.9% [25/194], $p < 0.05$) was observed in group A than group C. In terms of obstetrical complications, higher incidence of cesarean section (73.6 % vs. 49.5%, $P < 0.05$), postpartum hemorrhage (13.8% vs 2.1%, $p < 0.05$) and blood transfusion (28.9% vs 2.1%, $p < 0.05$) were observed in group A than group C. In Group A, 17.2 % (15/87) patients received intrauterine balloon pressure and 1 patient received subtotal hysterectomy to prevent further postpartum hemorrhage. In group C, only 3.7% (7/88) patients received intrauterine balloon pressure and no one underwent hysterectomy.

Other obstetrical outcomes, for example, ectopic pregnancy (3.1% vs. 0%, $P=0.065$), pregnancy-induced hypertension (8.2 vs. 2.7, $P=0.065$), gestational diabetes mellitus(20.7 % vs. 14.4%, $P=0.187$), placenta previa(4.6% vs. 1.1%, $P=0.155$), poor wound healing(3.4% vs. 0.5%, $P=0.181$) and less oligohydramnios (1.1% vs. 6.4%, $P=0.057$) seemed to be occurred in group A than group C, however no statistical significance were found.

In terms of liver-related disease, the rates of bleeding gums(7.2 % vs. 1.0%, $P < 0.05$), TBA elevation (18.6 % vs. 3.1%, $P < 0.05$), new ascites or aggravating ascites(6.2% vs. 0%, $p < 0.05$), MODS(7.2% vs. 0.5%, $P < 0.05$) and intensive care unit admissions(24.1% vs 1.1%, $P < 0.05$) were found in group A than group C. 10.3% infection (4 bacterial peritonitis, 1 chorioamnionitis, 1 fungi infection, 3 severe pneumonia and 1 intestinal infections) were observed in group A. However, only 1 case with upper tract infection were observed in group C ($P < 0.05$). **There were** no cases of maternal deaths but **2** cases of variceal bleeding in our study. One case was a tubal ectopic pregnancy and received laparoscopic Salpingectomy. 1 day later

she underwent variceal bleeding more than 1000ml. The other case underwent variceal bleeding during postpartum. 8 patients were diagnosed with esophageal varices before the third trimester and 5 patients received endoscopic treatment or pericardial devascularization before delivery. One patient developed progressive jaundice at 8 weeks, and progressive disturbance of consciousness after a fall at 22 weeks, MRI indicated subdural hematoma and subarachnoid hemorrhage. She was recovered and delivered after treatment.

In terms of fetal/infant complications, a significantly higher frequency of preterm delivery (30.7% vs. 4.2%, $p=6.89 \times 10^{-10}$), low birth weight infant (13.6% vs. 2.6%, $P=3.88 \times 10^{-4}$), asphyxia of newborn (10.2% vs. 1.1%, $P=9.42 \times 10^{-4}$), neonatal ICU admission (9.1% vs. 1.6%, $P=0.008$) and fetal/newborn death (4.5% vs. 0%, $P=0.016$) in group A than in group C. The intrauterine fetal death were occurred at 31.29 ± 6.02 weeks.

The Outcomes of the patients with liver cirrhosis continued pregnancy or not

The clinical characteristics of the liver cirrhosis patients who continued the pregnancy or not were summarized in suppl Table 1. Compared to the patients who chose to continue the pregnancy, patients who discontinued the pregnancy for concerning the disease deteriorated had more history of gravidity (89.6% vs. 63.9%) and multipara (79.3% vs. 33%). More women in group B had Hypersplenism (thrombocytopenia or anemia) than group B (54.6% vs. 79.3%, $P=0.017$). The lower level of PLT (85.34 ± 54.49 vs. 123.52 ± 66.66 , $p=0.006$), PTA (89.56 ± 11.50 vs. 96.79 ± 17.27 , $p=0.036$) and a higher level of Albumin (41.81 ± 5.00 vs. 39.49 ± 5.22 , $p=0.036$) were found in group B than group A. Compared to women who chose to discontinue the pregnancy, women in group B had more severe negative outcomes (32.0 vs. 3.4, $P=0.002$).

The predictors of severe negative outcomes in patients who had liver cirrhosis and progressed into the third trimester

To investigate the predictors of severe negative outcomes in this population, we performed multivariate classification logistic regression analysis to compare the baseline variables. Patients with severe negative outcomes had a higher CTP scores (OR= 2.128, 95% CI: [1.002, 4.521] , $p=0.049$) . Besides, patients with liver cirrhosis caused by Wilson's disease had a better prognosis than by HBV infection (OR= 0.009, 95% CI: [0, 0.763], $p=0.038$). No other predictors of negative maternal outcomes were found with a significant difference in baseline values (suppl Table 2).

Discussion/conclusion

Pregnancy and liver cirrhosis are a high-risk combination. The risks for the mother and the fetus are associated with worsening of liver decompensation and progression of portal hypertension: ascites, hepatorenal syndrome, hepatic encephalopathy, and variceal hemorrhage¹⁰. Though most of our patients were in the compensatory stage, patients with liver cirrhosis have a significantly lower level of platelet, hemoglobin, prothrombin activity, and a higher level of ALT, Total Bilirubin, and Creatinine. The incidence

of spontaneous abortions and abnormal uterine bleeding were increased as the progression of liver cirrhosis¹⁰. However, no difference in missed abortion and spontaneous abortion were found between pregnant patients with cirrhosis or not in our study.

The maternal death rates had decreased from 10% to 1%~1.8% as the medical therapy developing^{3,11-12}. In the previous study, the majority of maternal mortality was attributed to hemorrhage from gastrointestinal varices, occurring most commonly in the second trimester and during labor^{9,13}. There were no cases of maternal deaths but 2 cases of variceal bleeding in our study. One of them might be caused by laparoscopic pneumoperitoneum and stress of surgery. However, the obstetric complications were still 61% in women with cirrhosis, which was higher than 12% in the control group⁷. In our study, liver cirrhosis has a similar higher frequency of severe negative outcomes (32.0% vs 1.5%) than control. The most common negative outcomes in our study were bleeding gums, TBA, cesarean section, postpartum hemorrhage, new ascites, or aggravating ascites and MODS. 24.1% patients need intensive care unit admissions and 28.9% patients need blood transfusion. Except for these risks, we found more subclinical hypothyroidism during pregnancy (7.2% vs. 3.1%), pregnancy-induced hypertension (8.2% vs. 2.7%), GDM (20.7% vs. 14.4%) seemed to occur in patients with liver cirrhosis which might be associated with the poor liver metabolism. However, no statistically significant differences were found. Besides, patients with liver cirrhosis had more placenta previa (4.6% vs. 1.1%), and less oligohydramnios (1.1% vs. 6.4%) which were related to more preterm delivery (30.7% vs. 4.2%). More TBA elevation (18.6% vs. 3.1%) or preterm delivery might be associated with the higher asphyxia of newborn (10.2% vs. 1.1%) and fetal/newborn death (4.5% vs. 0%) in the liver cirrhosis patients.

The main etiological causes of cirrhosis in this study were viral hepatitis which accounted for 86.6% of all diagnoses. This differs from previous studies in which alcoholic liver disease was the main underlying cause of liver disease. This likely reflects a difference in the prevalence of liver disease in these populations¹⁴⁻¹⁶. In our study, patients with liver cirrhosis caused by Wilson's disease had a better prognosis than by HBV infection. Patients with severe negative outcomes had a higher CTP score. Other factors such as age, the duration of disease, history of delivery, and portal hypertension, and mode of delivery did not predict the severe negative outcomes well independently. Compared to women who continue the pregnancy, women who chose to discontinue the pregnancy in the first trimester could avoid the most severe negative outcomes. Then, the management of those patients should be individual. The patients with a higher CTP score should be advised to discontinue the pregnancy in the first trimester.

Given the retrospective nature of our study, we were unable to determine the long-time outcomes of liver cirrhosis. Besides, for the sample size confined, the effect on some pregnancy-related disease are not clear, such as hypothyroidism, GDM, and PIH. And further multicenter comparative studies were.

In this study, we found that the frequency of the severe negative outcomes (including liver-related complications, obstetrical complications, and fetal or neonatal death) was significantly increased in pregnancies complicated by cirrhosis. The predictor of severe negative outcomes is higher CTP score and

Wilson's disease induced liver cirrhosis have a better prognosis. Timely terminate the pregnancy during the first trimester may avoid the incidence of those severe negative outcomes.

Declarations

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments. The study design was reviewed and approved by the Ethics Committee of Beijing YouAn Hospital, Capital Medical University (approval number: Jing-you-ke-lun-zi [2020]050-hao). Permission to access and to use these data was approved by the institution. The need for informed consent was waived.

Consent for publication: Not applicable.

Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interest: The authors declare that they have no conflict of interest.

Funding: This study was supported by Beijing Hospitals Authority Talent Training Plan (grant number: QMS20191701).

Author Contributions

Drs. Wang and Zhu proposed the concept and designed the study. Drs. Zhu and Wang obtained the research funding. Drs Gao and Wang contributed to the acquisition of data. Dr. Zhu supervised the data collection. Drs. Wang performed the statistics. Drs. Wang interpreted the data and wrote the manuscript. All authors provided inputs for the manuscript.

References

1. Schuppan D, Afdhal NH. Liver cirrhosis. *Lancet*. 2008;371(9615):838-851.
2. Bell H, Raknerud N, Falch JA, Haug E. Inappropriately low levels of gonadotrophins in amenorrhoeic women with alcoholic and non-alcoholic cirrhosis. *Eur J Endocrinol*. 1995;132(4):444-449.
3. Shaheen AA, Myers RP. The outcomes of pregnancy in patients with cirrhosis: a population-based study. *Liver Int*. 2010;30(2):275-283.
4. Tan J, Surti B, Saab S. Pregnancy and cirrhosis. *Liver Transpl*. 2008;14(8):1081-1091
5. Hagström H, Höijer J, Marschall HU, et al. Outcomes of Pregnancy in Mothers with Cirrhosis: A National Population-Based Cohort Study of 1.3 Million Pregnancies. *Hepatol Commun*. 2018;2(11):1299-1305.
6. Zeeman GG, Moise KJ Jr. Prophylactic banding of severe esophageal varices associated with liver cirrhosis in pregnancy. *Obstet Gynecol*. 1999;94(5 Pt 2):842.

7. Palatnik A, Rinella ME. Medical and Obstetric Complications Among Pregnant Women with Liver Cirrhosis. *Obstet Gynecol.* 2017;129(6):1118-1123.
8. Puljic A, Salati J, Doss A, Caughey AB. Outcomes of pregnancies complicated by liver cirrhosis, portal hypertension, or esophageal varices. *J Matern Fetal Neonatal Med.* 2016;29(3):506-509.
9. Rasheed SM, Abdel Monem AM, Abd Ellah AH, Abdel Fattah MS. Prognosis and determinants of pregnancy outcome among patients with post-hepatitis liver cirrhosis. *Int J Gynaecol Obstet.* 2013;121(3):247-251.
10. Kotzev AI, Tanchev LS, Pavlov CS, Tanchev SY. *Ter Arkh.* 2019;91(4):114-117.
11. Lelei-Mailu FJ, Mariara CM. Pregnancy in a patient with portal hypertension secondary to liver cirrhosis. *BMJ Case Rep.* 2018;2018: bcr2017223076.
12. Murthy SK, Heathcote EJ, Nguyen GC. Impact of cirrhosis and liver transplant on maternal health during labor and delivery. *Clin Gastroenterol Hepatol.* 2009;7(12):1367-1372.e1.
13. Hay JE. Liver disease in pregnancy. *Hepatology* 2008;47: 1067–76
14. 14. Puljic A, Salati J, Doss A, Caughey AB. Outcomes of pregnancies complicated by liver cirrhosis, portal hypertension, or esophageal varices. *J Matern Fetal Neonatal Med.* 2016;29(3):506-509.
15. Pfeiffenberger J, Beinhardt S, Gotthardt DN, et al. Pregnancy in Wilson's disease: Management and outcome. *Hepatology.* 2018;67(4):1261-1269.
16. Milić S, Tatalović T, Mikolašević I. Pre-existing liver disease in pregnancy: Cirrhosis, autoimmune hepatitis and liver transplantation. *Best Pract Res Clin Gastroenterol.* 2020;44-45:101668.

Tables

Table 1. Baseline characteristics of mothers with and without liver cirrhosis(n=291)

	Group A (n= 97)	Group C (n=194)	t/χ²/Z, P
Age (mean±SD, years)	30.79± 5.01	31.38± 4.13	t=0.993, p=0.322
Gravidity, n (%)			
1	35(36.1)	78(40.2)	Z=0.555, p=0.579
2	30(30.9)	55(28.4)	
>2	32(33)	61(31.4)	
Multipara, n (%)	32(33)	83(42.8)	χ ² =2.595, P=0.107
Lab on first visit (mean±SD)			
Platelet (*10 ⁹ /L)	123.51±66.66	239.60±54.70	t=15.638, p=4.34*10 ⁻⁴⁰
Hemoglobin(g/L)	117.37±14.91	124.97±14.13	t=4.191, p=3.7*10 ⁻⁷
ALT(IU/L)	43.38±60.49	20.74±21.42	t=3.539, p=5.98*10 ⁻⁴
Albumin(g/L)	39.49±5.22	43.85± 27.17	t=1.549, p=0.123
Total Bilirubin(umol/L)	20.35±39.31	11.00±6.78	t=2.302, p=0.023
Prothrombin activity (%)	96.79±17.27	105.87±11.14	t=4.579, p=1.0*10 ⁻⁵
Creatinine(umol/L)	45.72±7.49	43.00±6.65	t=3.084, p=2.25*10 ⁻³

ALT, alanine aminotransferase.

Table 2. Negative maternal and fetal/infant outcomes in mothers with and without liver cirrhosis(n=291)

	Group A	Group C	t/ χ^2 , P-value
Maternal Complications, n (%)	(n=97)	(n=194)	
First trimester	n=97	n=194	
Ectopic pregnancy	3(3.1)	0(0)	$\chi^2=3.41$, P=0.065
Induced abortion	1(1)	0(0)	P**=0.33
Missed abortion	4(4.1)	6 (3.1)	$\chi^2=0.013$, P=0.91
Subclinical hypothyroidism during pregnancy	7(7.2)	6(3.1)	$\chi^2=1.71$, P=0.19
Second trimester	n=89	n=188	
Spontaneous abortion	2(2.2)	0(0)	P**=0.10
Pregnancy-induced hypertension	8(8.2)	5(2.7)	$\chi^2=3.39$, P=0.065
Third trimester	n=87	n=188	
Gestational diabetes mellitus	18(20.7)	27(14.4)	$\chi^2=1.74$, P=0.19
Intrauterine fetal death	3(3.4)	0(0)	P**=0.031
Oligohydramnios	1(1.1)	12(6.4)	$\chi^2=3.62$, P=0.057
Placenta Previa	1+3 (4.6)	2(1.1)	$\chi^2=2.02$, P=0.16
Placenta abruption	1(1.1)	1(0.5)	P**=0.55
Cesarean section	64(73.6)	93(49.5)	$\chi^2=14.10$, P=1.7*10 ⁻⁵
Postpartum	n=87	n=188	
Postpartum Hemorrhage	12 (13.8)	4(2.1)	$\chi^2=14.77$, P=1.2*10 ⁻⁴
Intensive care unit admission	21(24.1)	2(1.1)	$\chi^2=41.32$, P=1.3*10 ⁻¹⁰

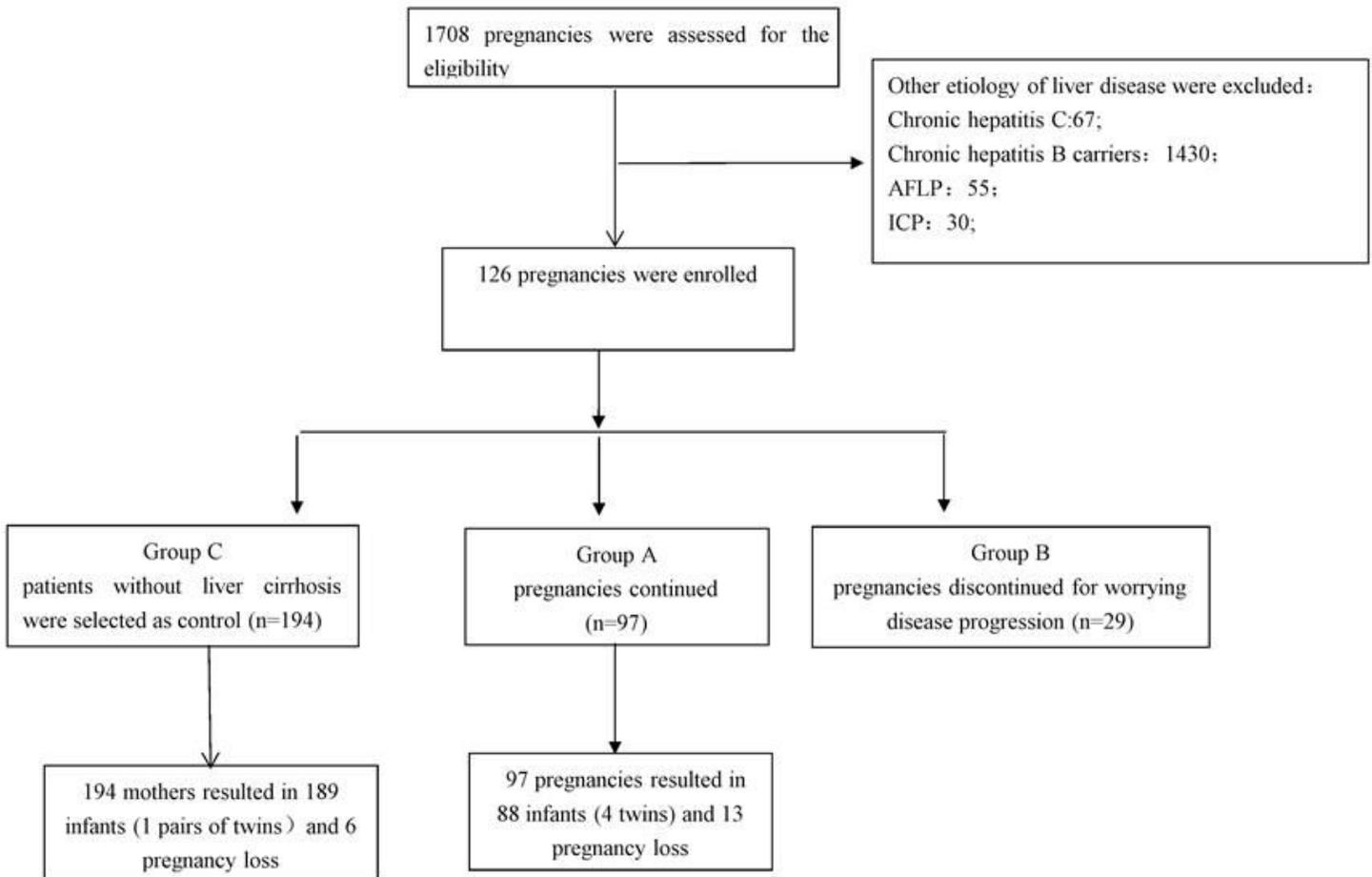
Intrauterine balloon pressure	15(17.2)	7(3.7)	$\chi^2=14.77$, $P=1.2*10^{-4}$
Hysterectomy	1(1)	0(0)	$P^{**}=0.33$
Poor wound healing	3(3.4)	1(0.5)	$\chi^2\#=1.79$, $p=0.18$
Complication due to liver-related events	n=97	n=194	
Bleeding Gums	7(7.2)	2(1.0)	$\chi^2\#=6.32$, $p=0.012$
Infection	10(10.3)	1(0.5)	$\chi^2=14.47$, $p=1.4*10^{-4}$
MODS	7(7.2)	1(0.5)	$\chi^2\#=8.50$, $p=4.0*10^{-3}$
Right heart failure	1(1.0)	0(0)	$p^{**}=0.33$
Respiratory failure	1(1.0)	0(0)	$p^{**}=0.33$
Acute liver failure	2(2.1)	0(0)	$p^{**}=0.11$
Renal insufficiency	3(3.1)	1(0.5)	$\chi^2\#=1.55$, $p=0.21$
Subarachnoid hemorrhage	1(1.0)	0(0)	$p^{**}=0.33$
Coagulation disorders	2(2.1)	1(0.5)	$\chi^2\#=0.38$, $p=0.54$
New ascites or aggravating ascites	6(6.2)	0(0)	$\chi^2\#=9.38$, $p=2.0*10^{-3}$
Upper gastrointestinal hemorrhage	2(2.1)	0(0)	$p^{**}=0.11$
TBA elevation	18(18.6)	6(3.1)	$\chi^2=20.43$, $p=6.0*10^{-6}$
ALT elevation			
Mild	16(16.5)	4(2.1)	$Z=6.898$, $p=5.3*10^{-12}$
Moderate	13(13.4)	2(1.0)	
Severe	2(2.1)	0(0)	

Blood Transfusion	28(28.9)	4(2.1)	$\chi^2=47.47$, $p=5.6*10^{-12}$
Severe negative outcomes	31(32.0)	3(1.5)	$\chi^2\#=57.964$, $p=2.7*10^{-14}$
Fetal/newborn complications , n (%)	(n=88)	(n=189)	t/χ^2, P-value
Gestational weeks of delivery (mean \pm SD, weeks)	37.62\pm2.63	39.07\pm1.53	t=4.75, p=6.0*10⁻⁶
Fetal development restriction	1(1.1)	2(1.1)	$\chi^2\#=0$, p=1
Low birth weight infant	12(13.6)	5(2.6)	$\chi^2=12.59$, $p=3.9*10^{-4}$
Fetal macrosomia	8(9.1)	10(5.3)	$\chi^2=1.43$, p=0.23
Fetal distress	4(4.5)	4(2.1)	$\chi^2\#=0.55$, p=0.46
Preterm delivery	27(30.7)	8(4.2)	$\chi^2=38.05$, $p=6.9*10^{-10}$
Asphyxia of newborn	9(10.2)	2(1.1)	$\chi^2=10.94$, $p=9.4*10^{-4}$
Apgar score 4-7 at 1min	4	1	
Apgar score 0-3 at 1min	5	1	
Neonatal ICU admission	8(9.1)	3(1.6)	$\chi^2\#=7.01$, $p=8.0*10^{-3}$
Fetal/newborn death	4(4.5)	0(0)	$\chi^2=5.82$, p=0.016

ALT, alanine aminotransferase; TBA, total bile acid; MODS, multiple organ dysfunction; ICU, intensive care unit. #continuous correction; ** Fisher's test.

Figures

Figure 1. Disposition of Mothers and Infants



AFLP: Acute fatty liver of pregnancy; ICP: intrahepatic cholestasis pregnancy.

Figure 1

Disposition of Mothers and Infants

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [suppltable2predictorofseverenegativeoutcome.doc](#)
- [suppltable1groupAvs.B.doc](#)