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CLINICAL ARTICLE

Maternal and perinatal outcome in cases of fulminant viral hepatitis in late pregnancy

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ABSTRACT

Objective: To investigate maternal and perinatal outcomes in cases of fulminant viral hepatitis in late pregnancy (FVHILP). *Methods:* A multicenter retrospective study was conducted. The records of 40 patients with FVHILP were retrieved from 3 hospitals in China. To analyze the influence of mode of delivery on maternal and perinatal outcomes, women were allocated to the cesarean delivery group or the spontaneous vaginal delivery (SVD) group. To study the relationship between maternal outcome and perinatal outcome, patients were allocated to the maternal survival group or the non-survival group. *Results:* There were no significant differences between the cesarean group and the SVD group in clinical manifestations or laboratory indices before delivery, or in fatality rate ($P>0.05$ for all), whereas there were significant differences in newborn weight, 1-minute Apgar score, and incidence of severe perinatal asphyxia between the maternal survival group and the non-survival group ($P<0.05$ for all). *Conclusion:* Maternal and perinatal outcomes in cases of FVHILP were not influenced by mode of delivery, whereas perinatal outcome significantly correlated with maternal outcome.

1. Introduction

Fulminant viral hepatitis in pregnancy is a rare disease characterized by acute onset, rapid progression, complicated clinical symptoms, and high fatality rate [1–4]. The condition is seen most often in patients infected with hepatitis B virus (HBV) or hepatitis E virus in low-resource countries in Asia and Africa, with a reported maternal fatality rate of 56%–75% and a perinatal mortality rate of 37%–49% [5,6]. Patients with fulminant viral hepatitis in late pregnancy (FVHILP), which occurs at 28 weeks of gestation or later, often present with coagulation disorders, hepatic encephalopathy, hepatorenal syndrome, paralytic ileus, and infection [7,8].

Because of the low incidence of FVHILP, only a few studies analyzing the prognosis of the condition are available [1,9,10]. The aim of the present study was to investigate the influence of mode of delivery on maternal and perinatal outcomes, in addition to determining the relationship between maternal and perinatal outcomes.

2. Materials and methods

A retrospective study of patients with FVHILP associated with HBV infection (serum hepatitis B surface antigen and/or HBV DNA positive) was conducted. The records of affected patients who were admitted and delivered at the Third Affiliated Hospital of Sun Yat-sen University (n = 19), Shanghai Public Health Clinical Center & Public Health Clinical Center Affiliated to Fudan University (n = 8), and the Third Affiliated Hospital of Guangzhou Medical College (n = 13), China, between January 1, 2000, and June 31, 2011, were consecutively retrieved. Approval for the study was obtained from the institutional ethics committee of each of the study hospitals.

All patients met the Chinese Medical Association clinical diagnostic criteria of fulminant viral hepatitis before delivery [11]. Patients were excluded if they had other virus co-infections or other pre-existing medical conditions (except hepatitis-related diseases), surgery (acute abdomen) during pregnancy, or additional pregnancy-specific liver diseases (acute fatty liver of pregnancy; intrahepatic cholestasis of pregnancy; pre-eclampsia; or hemolysis, elevated liver enzymes, and low platelet count [HELLP] syndrome) [4]. Patients were also excluded if fetal anomalies were detected, in order to exclude the false perinatal mortality rate due to such anomalies. Principles of treatment were comparable among all study hospitals during the period investigated, including dynamic monitoring (comprehensive physical exams and blood tests), supportive therapy (from several hours to several days,

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involving treatments such as intensive care unit [ICU] input; replenishment of serum albumin and globulin; restoration of coagulation function; and reduction of transaminases and toxins using herbal medicines [*Ganlixin* injection, the major content of which is diammonium glycyrrhizinate]) [12], antiviral medication (lamivudine), and symptom-relieving treatment. Indications for delivery included 1 or more of the following [11]: full-term pregnancy (≥37 weeks of gestation), with the patient receiving supportive treatment and with clinical symptoms and signs (including laboratory indices such as coagulation function, serum albumin, transaminase, and total bilirubin) remaining steady for 24–48 hours (n = 6); fetal distress if the fetus was viable (more than 28 weeks of gestation) (n = 12, with 2 twin pregnancies and 1 triplet pregnancy); no improvement in clinical condition after active treatment with medication, with the condition deteriorating (e.g. deterioration of hepatic encephalopathy) (n = 11) [7,13]; patient in labor (n = 11, with 1 twin pregnancy).

Cesarean under general anesthesia was the preferred mode of delivery; vaginal delivery was considered for patients who had already entered the labor process and in whom the cervix was mature and delivery was imminent [11,14]. Peripartum subtotal hysterectomy was performed in cases of intractable postpartum hemorrhage [15]. If necessary, viable newborns received neonatal resuscitation, and live newborns were transferred to the neonatal ICU (NICU) of the corresponding hospital.

Data on maternal and perinatal outcomes (death, complications, and evaluation of newborns) were retrospectively collected and compared between different delivery groups. Comparisons between the groups were carried out for clinical data at admission, including liver function and blood coagulation indices such as aspartate aminotransferase, alanine aminotransferase, and their ratio; albumin; total cholesterol (Tch); serum total bilirubin; prothrombin activity (PTA); cholinesterase; serum creatinine (Scr); blood glucose; and white blood cell count (WBC). Also compared were major complications such as hepatic encephalopathy, hepatorenal syndrome, disseminated intravascular coagulation, bleeding (obstetric hemorrhage, upper gastrointestinal bleeding, brain hemorrhage, and abdominal hematoma), and infections (peritoneal, uterine, pelvic, biliary, and urinary). The relationship between maternal and perinatal outcomes was also evaluated.

Measurement data were expressed as mean ± SD or median. Quantitative data were compared via Student *t* test or rank-sum test. The χ^2 test was used to analyze enumeration data. Statistical analyses were carried out using SPSS version 15.0 (IBM, Armonk, NY, USA). For all comparisons, $P<0.05$ in any 2-sided statistical test was considered to be statistically significant.

3. Results

The clinical characteristics of 40 eligible patients were analyzed. All patients were Han Chinese and from east or south China. Average maternal age at delivery was 27.2 ± 4.2 years, and mean gestational age at delivery was 35.3 ± 2.9 weeks. There were 3 twin pregnancies and 1 triplet pregnancy. There were no cases of HIV infection, hepatocellular carcinoma, or prior FVHILP history. Transfusion or infusion of blood-derived medicine was carried out after delivery in all cases as treatment for coagulation dysfunction. All women were admitted to the ICU, either before or after delivery. All cases involved infection with HBV only. Average time between onset of fulminant viral hepatitis and delivery was 14.5 ± 14.1 days. Twenty-seven women experienced complete recovery or an improvement in clinical conditions at discharge (mother survived at 6 months: survival group), with an average hospital stay of 30 ± 21 days. Thirteen women died or experienced a deterioration in clinical conditions at discharge (confirmation of maternal death within 6 months: non-survival group), with an average hospital stay of 8 ± 8 days. The total maternal fatality rate was 32.5%. Of the 45 newborns, 36 survived and 9 died, giving a mortality rate of 20.0%.

There were 8 spontaneous vaginal deliveries (SVDs) and 32 cesarean deliveries. There were no significant differences in blood test results between the SVD group and the cesarean group (Table 1). There were 14 (43.8%) cases involving 3 or more complications in the cesarean group, and 4 (50.0%) such cases in the SVD group ($P = 0.938$). The similar pre-delivery clinical parameters in the SVD and cesarean groups enabled the influence of delivery on maternal and perinatal outcomes to be analyzed without bias.

Table 1
Comparison of pre-delivery blood indicators between cesarean and spontaneous vaginal delivery groups.[a]

	Cesarean delivery	Spontaneous vaginal delivery	*t* value	*P* value
AST/ALT ratio	1.55 ± 0.74	1.37 ± 0.48	0.662	0.512
TBIL, μmol/L	222.09 ± 88.50	300.60 ± 142.08	1.976	0.056
Alb, g/L	25.90 ± 4.75	27.49 ± 3.32	0.888	0.380
Tch, mmol/L	2.58 ± 0.98	2.51 ± 1.08	0.157	0.876
Cr, mmol/L	112.67 ± 78.14	87.35 ± 61.28	0.850	0.400
PTA, %	31.47 ± 13.56	28.29 ± 24.21	0.496	0.642
CHE, IU/L	3405.76 ± 804.68	3759.17 ± 1250.14	0.860	0.397
Bs, mmol/L	5.02 ± 3.58	4.97 ± 4.49	0.035	0.972
WBC, $\times 10^9$/L	11.56 ± 3.51	13.26 ± 5.11	1.114	0.272

Abbreviations: Alb, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Bs, blood glucose; CHE, cholinesterase; PTA, prothrombin activity; Scr, serum creatinine; TBIL, serum total bilirubin; Tch, total cholesterol; WBC, white blood cell count.
[a] Values are given as mean ± SD unless otherwise indicated.

In the SVD group, 5 (62.5%) mothers survived, and 5 (62.5%) newborns survived and remained alive. In the cesarean group, which included 3 cases of twin pregnancy and 1 case of triplet pregnancy, 22 (68.8%) mothers survived and 31 (83.8%) newborns survived. There were no significant differences between the groups in maternal fatality rate ($P = 0.933$), postpartum hemorrhage ($P = 0.937$), infection ($P = 0.693$), hepatic encephalopathy ($P = 0.936$), or hepatorenal syndrome ($P = 0.804$) (Table 2). Subtotal hysterectomy was performed in 13 cases (5 in the non-survival group [all during cesarean delivery] and 8 in the survival group [7 during cesarean and 1 after SVD]). There were higher rates of perinatal death ($P = 0.380$) and severe asphyxia ($P = 0.638$) in the SVD group than in the cesarean group but the difference was not significant (Table 3).

The 45 perinatal outcomes were analyzed according to the associated maternal outcomes. Twenty-nine newborns from 27 mothers who survived after delivery (including 2 twin pregnancies) were allocated to the maternal survival group; 16 newborns from 13 mothers who died after delivery (including 1 twin and 1 triplet pregnancy) were allocated to the maternal non-survival group. There were significant differences in birth weight ($P = 0.003$), 1-minute Apgar score ($P = 0.025$), and severe asphyxia ($P = 0.045$) between the 2 groups (Table 4). Thirteen live newborns from 11 women, including 4 newborns from 2 cases of twin pregnancy and 1 newborn from a triplet pregnancy, were admitted to the NICU. Twenty-three live newborns were not admitted to the NICU. The other 9 cases involved fetal death or stillbirth, including 2 fetal deaths from a triplet pregnancy.

Table 2
Maternal outcomes according to delivery group.[a]

	Spontaneous vaginal delivery (n = 8)	Cesarean delivery (n = 32)	χ^2 value	*P* value
Maternal death	3 (37.5)	10 (31.3)	0.007	0.933
Postpartum hemorrhage	5 (62.5)	17 (53.1)	0.006	0.937
Infection	4 (50.0)	16 (50.0)	0.156	0.693
Hepatic encephalopathy	4 (50.0)	19 (59.4)	0.006	0.936
Hepatorenal syndrome	2 (25.0)	12 (37.5)	0.062	0.804
Previous parity	1.75 ± 0.71	2.06 ± 1.29	–	0.516 [b]

[a] Values are given as number (percentage) or mean ± SD unless otherwise indicated.
[b] *t* test.