Cirrhosis and Pregnancy: A Single Centre Experience

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Research Article

Keywords: Cirrhosis, pregnancy, hepatitis B

Posted Date: February 2nd, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1311018/v1

Abstract

Purpose

Cirrhosis is a diffuse pathology characterized by fibrosis of the liver and is the last stage of chronic liver diseases. It is a serious medical condition which seriously impacts reproduction and reproductive life span.

Methods

Retrospective chart review of the fetal and maternal results of 20 pregnant women with liver cirrhosis who had undergone antenatal follow-up and delivery at a tertiary center in a 12-year period was performed.

Results

Chronic hepatitis B was found to be the leading cause of liver cirrhosis in the study group, with a rate of 25 % (n: 5/20). The average MELD score was calculated as 8.8 ± 3.5. Only three patients developed hepatic decompensation during pregnancy. Fetal demise was observed in 10% of the cases (n: 2/20, MELD scores 8 and 17).

Conclusion

Even though pregnancy is rarely observed in women with liver cirrhosis, many patients with are able to achieve favorable maternal and fetal results without developing hepatic decompensation with appropriate management and close follow-up. The Model for End-Stage Liver Disease (MELD) score is a clinical tool utilized to estimate the severity and survival for chronic liver disease and was previously found to be associated with unfavorable outcomes in pregnant patients. Our study confirms this finding with the current experience from a tertiary care center. In addition, with the effects of cirrhosis on pregnancy being a concern, the impact of pregnancy on the course of the disease should also be addressed.

Introduction

Cirrhosis, the last stage of chronic liver diseases, is a diffuse pathology characterized by fibrosis, leaving the normal structure of the liver to abnormal non-organized regenerative nodules [1]. Pregnancy is rarely observed in women with liver cirrhosis overall. Possible causes of this epidemiological fact might be the onset of the disease at the post-menopausal period and the existence of disease-induced metabolic anomalies leading to anovulation and infertility in reproductive age women [2, 3]. However, recent studies reported increasing pregnancy and live birth rates in women with cirrhosis [4, 5].

The interaction between cirrhosis and the pregnancy is bilateral. As a chronic disease, the course and prognosis of cirrhosis is affected by the pregnancy, while the pregnancy is also impacted by cirrhosis. Many studies evaluated obstetric and fetal outcomes in pregnant women with cirrhosis, and reported an increase in abortion, fetal growth restriction, preterm delivery, perinatal mortality and cesarean delivery rates [6–8]. In addition, complications such as esophageal hemorrhage, liver failure, ascites, encephalopathy and postpartum hemorrhage were observed more frequently in pregnant women with cirrhosis [9–11]. In spite of the significant challenges in a pregnancy complicated by cirrhosis, a multi-disciplinary approach and well planned management by experienced providers might minimize the perinatal and maternal risks.

The aim of our study is to evaluate the fetal and maternal results of pregnant women with liver cirrhosis in a tertiary health centre in a 12-year period and review the results in the light of the existing literature.

Material And Methods

Pregnant women with liver cirrhosis who had their prenatal care and were delivered at the Department of Obstetrics and Gynecology at Ege University School of Medicine Hospital between 2008-2020 were evaluated retrospectively. The cases were initially identified by a computerized search with the diagnosis of “liver cirrhosis” (International Classification of Diseases 10th Revision Codes; K74.0, K74.1, K74.2, K74.3, K74.4, K74.5, K74.6) among pregnant women. Patients who did not attend prenatal visits regularly or with incomplete records were excluded from the study. The study was approved by the local ethics committee of Ege University School of Medicine.

The demographic features of pregnant women, age, parity, birth, delivery type, birth week, birth weight, 1st and 5th minute Apgar scores, indications were caesarean deliveries, anesthesia type, obstetric, maternal and fetal complications were obtained from antenatal follow-up files. Data regarding laboratory, imaging and endoscopy findings, pathology results and etiology of liver cirrhosis were also obtained.

Prenatal visits were scheduled as monthly in the first and second trimesters and weekly in the third trimester. Maternal complications were as follows: Ascites, esophageal variceal bleeding, encephalopathy, hepatorenal syndrome, splenic artery aneurysm rupture, gestational diabetes, hypertensive diseases of pregnancy (Preeclampsia, eclampsia, gestational hypertension, chronic hypertension, superimposed preeclampsia, HELLP syndrome), postpartum hemorrhage and venous thromboembolism. Obstetric complications were determined as follows: Preterm labor (<37 gestational week), preterm premature rupture of membranes (membrane rupture before 37 weeks), oligohydramnios, polyhydramnios, cesarean delivery, placental pathologies (placenta previa, placental detachment). Fetal complications: abortion, fetal death, congenital anomaly and fetal growth restriction (<10th percentile of birth weight for gestational age).

Serum samples were obtained at certain intervals according to the recommendations of the Gastroenterology department. Data on hemoglobin, platelet count, electrolytes, liver enzymes, bilirubin, albumin, creatinine, prothrombin time, international normalized ratio for prothrombin time (INR) value were evaluated.

The Model for End-Stage Liver Disease (MELD) scoring system is a prognostic model developed to predict the severity and survival of patients with chronic liver disease [12]. In our study group, MELD scoring was performed using the first trimester bilirubin, creatinine and INR values [13]. Numerical variables are given as mean and standard deviation or median (min-max). Categorical variables are given as numbers and percentages. Statistical analysis was not reported and multivariate analysis was not carried out due to the small sample size and significant results.

Results

During the study period, 20 pregnancies complicated by liver cirrhosis have been identified. Demographic data, obstetric features, maternal and fetal results of the patients are shown in detail in Table 1. Chronic hepatitis B was found to be the leading cause of liver cirrhosis in the study group, with a rate of 25% (n: 5/20). In 20% of cases, despite the comprehensive clinical, serological and pathological evaluation, etiology was not fully elucidated. The first trimester laboratory findings are detailed in Table 2. Anemia (hemoglobin <11 g / dL or hematocrit <33 percent) was observed in 55% of the cases (n: 11/20), and thrombocytopenia (platelet count <150,000 / microL) in 65% (n: 13/20). Model for End-Stage Liver Disease score was calculated using the first trimester serum bilirubin, creatinine and INR values. The average MELD score was calculated as 8.8 ± 3.5.

Table 1
Demographic data, obstetric features, maternal and fetal results of the patients

	Age	Etiology of cirrhosis	Delivery week	Delivery mode¥	Anesthesia	APGAR score 5 min	Obstetric complications	Maternal complications*	Fetal status	MELD score
1	32	Alcohol	35	CS(OB)	GA	9	Placenta previa PD	-	LB	6
2	37	CHB	20	TA(I)	-	-	-	-	IUFD	8
3	30	CC	38	CS(OB)	GA	10	-	-	LB	8
4	38	AH	13	TA(I)	-		-	Ascites, PPH	T	9
5	26	WD	15	TA(I)	-				IUFD	17
6	26	CHB	36	CS(M)	CSEA	10	PD		LB	6
7	35	PBC	35	CS(OB)	S	9	Polyhydramnios PD		LB	6
8	30	AH	37	CS(M)	S	10	-		LB	14
9	24	CC	37	CS(UK)	GA	8	Olygohydramnios	PPH	LB	10
10	30	CC	19	TA(I)	-	-	-	-	T	10
11	31	CHB	35	CS(F)	S	8	Olygohydramnios PD		LB	6
12	26	AH	31	CS(F)	GA	8	PD	Ascites, PPH	LB	17
13	31	PBC	39	NSVD	-	10	-	-	LB	6
14	33	CHB	40	CS(UK)	S	10	-	-	LB	6
15	34	CC	36	NSVD	-	9	PD		LB	8
16	32	PSC	8	TA(D&C)	GA	-	-		T	6
17	22	PBC	18	TA(I)	-	-	-	Ascites	T	11
18	37	PSC	30	NSVD	-	8	PPROM, PD	GDM	LB	7
19	28	CHB	37	CS(OB)	S	9	-		LB	6
20	33	PBC	34	CS(M)	S	8	PD	GDM	LB	9

¥ Cesarean delivery: Followed by indications for cesarean delivery as fetal, maternal, obstetric, or unknown.

CHB: Chronic Hepatitis B, CC: Cryptogenic Cirrhosis, AH: Autoimmune Hepatitis, WD: Wilson disease, PBC: Primary Biliary Cholangitis, PSC: Primary Sclerosing Cholangitis, NSVD: Normal Spontaneous Vaginal Delivery, CS: Cesarean Section, OB: Obstetric Indication for Cesarean Delivery; F: Fetal Indication for Cesarean Delivery, M: Maternal Indication for Cesarean Delivery, U: Unknown, TA: Therapeutic Abortion, I: Induction, D&C : Dilation and Curettage, S: Spinal Anesthesia, CSEA:Combined Spinal-Epidural Anesthesia, GA: General Anesthesia, P: Preeclampsia, PD: Preterm Delivery, PPROM: Preterm Premature Rupture of Membranes, PPH: Postpartum Hemorrhage, GDM: Gestational Diabetes Mellitus, T: Terminated, IUFD: Intrauterine Fetal Death, LB: Live Birth

Table 2
Mean values of serum parameters in first trimester

	Value
Bilurubin (mg/dl)	1.33±1.2
Albumin(g/dl)	3.33±0.5
AST (IU/dl)	30.3±18
ALT (IU/dl)	26.4±23.9
Creatinine (mg/dl)	0.6±0.2
Hemoglobin (g/dl)	11.1±1.3
Platelet count (10^3/microL)	124±86
Protrombin time (sec)	11.5±2.1
INR	1.02±0.3
MELD score	8.8±3.5
AST: Aspartate Transaminase, ALT: Alanine Transaminase, INR: International Normalized Ratio, MELD: The Model for End-Stage Liver Disease	
Values are given as mean±SD	

Only three patients developed hepatic decompensation during pregnancy. Ascites was noteworthy in all patients with decompensation and MELD score was found to be 9,17 and 11, respectively. In two cases with hepatic decompensation, pregnancy was terminated with the recommendation of Gastroenterology and in compliance with the family request. The third case decided to pursue the pregnancy until 31 weeks and was delivered with cesarean section due to fetal distress. Six patients had a history of variceal hemorrhage before pregnancy and none of the cases had variceal bleeding or any other morbidity during their pregnancies. No mortality has been observed until July 2020 and liver transplantation from cadaver was performed in two cases independent of the pregnancy status.

Fetal demise was observed in 10% of the cases (n: 2/20, MELD scores 8 and 17). In 20% (n: 4/20, MELD score, respectively, 9,10,6,11) of cases, termination of the pregnancy was performed according to the suggestions of gastroenterology and the request of the patient. The remaining 14 cases resulted in live birth. Among these, the mean gestational week at delivery was 35.7 ± 2.7 and the premature delivery rate was 42.8% (n: 6/14). The cesarean delivery rate is 78.5% (n: 11/14). Vaginal delivery was performed in three cases and neither induction nor neuroaxial blockade was applied. 36% of caesarean sections were performed due to obstetric indications, whereas 27% were due to maternal and 18% were due to fetal indications. In cases delivered by cesarean section, regional anesthesia was mostly preferred. (63.6% n: 7/11). Six patients with a platelet count below the critical value (<50,000/microL) received prophylactic platelet transfusion. Postpartum hemorrhage was observed in only three cases which were successfully managed medically and with blood transfusion. No fetal anomaly was found in any case resulted in live birth, and only one case was complicated with fetal growth restriction.

Discussion

In our study, the maternal and fetal outcomes of 20 pregnancies complicated by liver cirrhosis performed in a single healthcare institution between 2008 and 2020 were evaluated. Liver cirrhosis is a histopathologically defined, life threatening, chronic and progressive condition. Determining the etiology is crucial in terms of managing the disease as well as providing counselling regarding the prognosis of the pregnancy. The etiology of liver cirrhosis also varies according to the economic status of the countries. Alcoholic liver disease, chronic hepatitis C and non-alcoholic fatty liver disease make up 80% of patients waiting in line for a liver transplant in the United States. [14]. Chronic hepatitis B is the most prevalent diagnosis among our patient population. While many women with liver cirrhosis may be able to pursue their pregnancies without hepatic compromise, some women may show signs of hepatic decompensation, such as ascites, variceal bleeding, encephalopathy, and hepatorenal syndrome [15]. Previous

studies reported that the rate of decompensation in pregnant women with liver cirrhosis was 24% and variceal bleeding rate was 32%, while Shaheen et al. reported a decompensation rate as 15%, ascites 11% and variceal bleeding as 5%[10, 16, 17]. In our study, decompensation was observed in 15% of the patient group, and the ascites was seen in all of these cases.

The increase in the total blood volume associated with pregnancy might worsen portal hypertension, and an increased risk of variceal bleeding is also observed, especially after the second trimester [16, 18]. Without timely diagnosis and management, it is an important cause of morbidity and mortality which can lead to catastrophic consequences. In the literature, maternal mortality rates due to liver cirrhosis during pregnancy vary between 10% and 61%, with the inclusion of earlier studies [9, 17, 19]. In our study, six patients had a history of variceal bleeding before pregnancy and none of the patients in the study encountered variceal bleeding and maternal mortality during pregnancy.

Various abnormalities in serum parameters can be seen in patients with liver cirrhosis. In addition, the disease may even manifest with these abnormalities. Some of the alterations include elevated serum bilirubin, aminotransferase, alkaline phosphatase, gamma-glutamyl transpeptidase, prolonged prothrombin time and INR values, as well as hyponatremia, anemia, and thrombocytopenia [20–22]. While thrombocytopenia is the most common hematological disorder, leukopenia and anemia may occur later in the disease [23] [24]. In our study, anemia was noted in 55% of patients, whereas thrombocytopenia was found in 65%. Preoperative prophylactic platelet transfusion was needed in approximately half of the cases with thrombocytopenia. While thrombocytopenia in cirrhosis patients is mostly due to congestive splenomegaly and portal hypertension, the development of anemia can be related to a variety of factors such as acute and chronic gastrointestinal blood loss, folate deficiency, alcohol-related toxicity, hypersplenism, anemia of chronic disease and hemolysis [23].

The Model for End-Stage Liver Disease (MELD) score is a clinical tool utilized to estimate the severity and survival for chronic liver disease [12]. In the study of Westbrook et al., the MELD score of 10 and above was associated with poor maternal results [11]. In our study, even though MELD score of 6 patients was 10 and above, the mean MELD score was 8.8. Patients with high MELD scores were associated with poor maternal and fetal outcomes.

The incidence of abortion, stillbirth and preterm delivery appears to be increased in pregnancies complicated by liver cirrhosis [10, 11]. Spontaneous abortion occurred in 10% of the cases and pregnancy was terminated in 20% of the patients. Preterm delivery rate was 42.8% and the indication for preterm deliveries were obstetric and fetal in majority of patients. There is still not enough evidence regarding the ideal delivery route in pregnancies complicated with cirrhosis. A theoretical increase in the risk of bleeding that may result from injuries to abdominal collaterals during the entry into the abdomen in cesarean section is likely. However, an increase in the risk of variceal bleeding due to increased abdominal pressure during vaginal deliveries is another concern. Due to the lack of consensus in the method of delivery, there are obvious differences among the studies reported in terms of cesarean delivery rates. In the study conducted by Rasheed et al., cesarean rate in pregnant women with cirrhosis was 91.5%, while it was reported as 26% in the study conducted by Palatnik et al [15, 24]. In our study, while cesarean delivery rate was 78.5%, most of the caesarean sections were performed due to obstetric indications. In addition, regional anesthesia was mostly preferred in cesarean deliveries due to its advantages on maternal cardiopulmonary and hemodynamic system.

It is important to emphasize that the limitations of our study include the number of the patients enrolled in the study and retrospective nature of the study.

According to the studies in the literature, many patients with chronic liver disease are able to achieve favourable maternal and fetal results without developing hepatic decompensation with appropriate management and close follow-up. Despite all these favourable advancements, termination of the pregnancy should be strongly considered in pregnant women with high risk of variceal bleeding or in the presence of symptoms concerning for hepatic decompensation. Pregnancy in patients with liver cirrhosis should be managed in a multidisciplinary approach, including a maternal-fetal medicine specialist, neonatologist and hepatologist.

Declarations

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Competing Interests

The authors declare no conflict of interest.

Author Contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [Metehan Imamoglu], [Huseyin Ekici], [Firat Okmen] and [Mete Ergenoglu]. The first draft of the manuscript was written by [Metehan Imamoglu], and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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