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Research Article
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Pregnancy outcomes in women with Budd–Chiari syndrome or portal vein thrombosis – a multicentre retrospective cohort study

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Objective To evaluate current practice and outcomes of pregnancy in women previously diagnosed with Budd–Chiari syndrome and/or portal vein thrombosis, with and without concomitant portal hypertension.

Design and setting Multicentre retrospective cohort study between 2008 and 2021.

Population Women who conceived in the predefined period after the diagnosis of Budd–Chiari syndrome and/or portal vein thrombosis.

Methods and main outcome measures We collected data on diagnosis and clinical features. The primary outcomes were maternal mortality and live birth rate. Secondary outcomes included maternal, neonatal and obstetric complications.

Results Forty-five women (12 Budd–Chiari syndrome, 33 portal vein thrombosis; 76 pregnancies) were included. Underlying prothrombotic disorders were present in 23 of the 45 women (51%). Thirty-eight women (84%) received low-molecular-weight heparin during pregnancy. Of 45 first pregnancies, 11 (24%) ended in pregnancy loss and 34 (76%) resulted in live birth of which 27 were at term (79% of live births and 60% of pregnancies). No maternal deaths were observed; one woman developed pulmonary embolism during pregnancy and two women (4%) had variceal bleeding requiring intervention.

Conclusions The high number of term live births (79%) and lower than expected risk of pregnancy-related maternal and neonatal morbidity in our cohort suggest that Budd–Chiari syndrome and/or portal vein thrombosis should not be considered as an absolute contraindication for pregnancy. Individualised, nuanced counselling and a multidisciplinary pregnancy surveillance approach are essential in this patient population.

Keywords Budd–Chiari Syndrome – portal vein thrombosis, counselling, pregnancy, thrombosis.

Tweetable abstract Budd–Chiari syndrome and/or portal vein thrombosis should not be considered as an absolute contraindication for pregnancy.

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Introduction

Budd–Chiari syndrome and portal vein thrombosis are unusual manifestations of venous thromboembolism. Budd–Chiari syndrome is a rare disorder and current knowledge on its epidemiology, aetiology and prognosis stems mainly from small observational studies.[1,2] It is defined as obstruction of the hepatic venous outflow predominantly caused by thrombosis of the hepatic veins or proximal inferior vena cava. Presence of portal hypertension and comorbidity form the major determinants of patient outcome.[3–5] Underlying prothrombotic disorders, such as myeloproliferative neoplasms, antiphospholipid syndrome and inherited thrombophilia, are common in Budd–Chiari syndrome.[1,2] Regardless of the underlying disorder, there is an indication for long-term anticoagulant therapy.[6–8] Concurrently, liver-dysfunction-associated coagulopathy, portal hypertension and gastrointestinal varices contribute to an increased bleeding risk in these patients.[8]

The prevalence of sex-specific transient risk factors, in particular use of oral contraceptives, is present in up to 40% of patients with Budd–Chiari syndrome.[1,4] Pregnancy as a risk factor could be identified in approximately 13% of Budd–Chiari syndrome patients in the few studies investigating this.[9,10] Women with Budd–Chiari syndrome have a higher incidence of primary infertility and adverse pregnancy outcomes compared with the general population.[11] Treatment of Budd–Chiari syndrome, including a portosystemic shunt or stent placement, may increase the probability of successful conception and pregnancy outcome.[11–13] Oesophageal variceal bleeding is the most feared complication during pregnancy in women with concomitant portal hypertension.[14,15]

Portal vein thrombosis, in the absence of hepatobiliary malignancy or cirrhosis, may be caused by an underlying prothrombotic state and/or a local inflammatory factor, and can lead to portal hypertension.[2,5,7,8] Conversely, portal vein thrombosis is one of the main complications in patients with non-cirrhotic portal hypertension.[15–17] In a recent multicentre European study, 45 pregnancies in 24 women with portal vein thrombosis were evaluated retrospectively.[16] The risk of pregnancy loss and preterm birth appeared to be increased, but favourable fetal and maternal outcomes were reported in 33 of 36 pregnancies reaching 20 weeks of gestation.

Because uncertainty exists regarding neonatal outcome and maternal morbidity, such as recurrent thrombosis and bleeding, there is no consensus on optimal management strategies throughout pregnancy for women with Budd–Chiari syndrome or portal vein thrombosis. Clinical practice with regard to preconception counselling is heterogeneous and some physicians still advise against pregnancy. We evaluated current practice and outcomes of pregnancy in women previously diagnosed with Budd–Chiari syndrome and/or portal vein thrombosis, with and without concomitant portal hypertension.

Methods

Study population and design

We performed a multicentre retrospective cohort study in four academic hospitals (Amsterdam UMC – location Academic Medical Centre, Amsterdam; Erasmus University Medical Centre, Rotterdam; University Medical Centre Groningen, Groningen; Radboud University Medical Centre, Nijmegen). The study protocol was approved by the medical ethics committee of the Amsterdam UMC – Academic Medical Centre in Amsterdam. Data were extracted from the electronic medical records from 1 January 2008 to 1 January 2021. Cases were identified using CTcue, a search engine designed for unstructured medical data. The search included the *International Classification of Diseases, Tenth Revision* codes as well as text words 'Budd–Chiari syndrome', 'Budd' or 'portal vein thrombosis' or 'portal vein' present anywhere in the medical records. Additionally, existing cohorts of known Budd–Chiari syndrome and/or portal vein thrombosis patients in each centre were checked and used to cross-reference cases identified in the search. We manually reviewed the electronic medical record for each case to ensure eligibility. The search was limited to women who were considering pregnancy, who were counselled regarding pregnancy or who had been pregnant after the diagnosis of Budd–Chiari syndrome and/or portal vein thrombosis. Concomitant presence of portal hypertension (defined as hepatic venous pressure gradient of 6 mmHg or more, or radiological findings suggesting portal hypertension, defined as splenomegaly, ascites, varices, portosystemic collaterals) was additionally assessed.

All data were retrieved from the electronic patient files. Women with a diagnosis of Budd–Chiari syndrome and/or portal vein thrombosis who were pregnant (confirmed by urine pregnancy test or ultrasound) after this diagnosis in the observational period, were included for analysis in the study. Exclusion criteria were ectopic pregnancy, a history of hepatobiliary malignancy or liver transplantation and pregnancies terminated for non-medical reasons. Approval for study conduct was obtained and eligible patients were contacted. The participants were not involved in the development of this study, and core outcome sets were not used. Study outcomes were assessed from conception up to 12 weeks after delivery or 6 weeks after pregnancy loss.

Outcomes

The primary outcomes were pregnancy-related maternal mortality and live birth rate. Secondary maternal outcomes

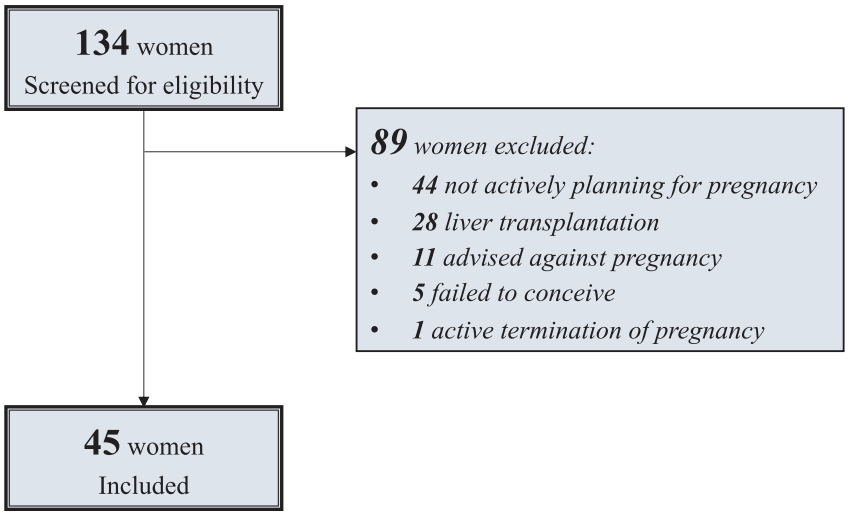

Figure 1. Flowchart of study screening and enrolment.

included hypertensive disorders of pregnancy (pre-eclampsia and pregnancy-induced hypertension[18]), arterial and venous thrombotic events, antepartum and postpartum bleeding events, and complications of pre-existent portal hypertension (oesophageal variceal bleeding, ascites). Secondary neonatal outcomes included gestational age at delivery, birthweight, small for gestational age (birthweight below the tenth centile and subgroup analysis below the third centile[19,20]), Apgar score less than 7 at 5 minutes, venous pH less than 7.21, asphyxia and admission to the neonatal intensive care unit.

Data on anticoagulant therapy and data on obstetric outcomes and complications, such as type and onset of delivery and postpartum haemorrhage, were also collected.

Statistical analyses

Descriptive statistics were used to summarize demographic and clinical characteristics. Primary and secondary outcomes were reported for all patients and separately for patients with Budd–Chiari syndrome (including those with concomitant portal vein thrombosis) and portal vein thrombosis. Additionally, we presented the outcomes for all pregnancies and for all first pregnancies, stratified per patient group.

The association between baseline characteristics and first pregnancy outcome, defined as pregnancy loss and any maternal adverse event, was assessed by means of a univariate logistic regression analysis and was expressed as odds ratios (OR) with corresponding 95% CI. All statistical analyses were carried out using the SPSS package (version 27.0, April 2020; IBM, Armonk, NY, USA).

Results

We identified 134 potentially eligible women with Budd–Chiari syndrome and/or portal vein thrombosis in the predefined study period. All women contemplating or actively planning for pregnancy were seen by a gynaecologist and underwent preconception counselling. All cases were discussed in multidisciplinary meetings before pregnancy and during pregnancy. Eleven women (8%) were advised against pregnancy and five (4%) failed to conceive. One woman unintendedly became pregnant and was advised to terminate the pregnancy as the potential risks were considered too high. Figure 1 provides an overview of the study screening process and reasons for exclusion.

Forty-five included women conceived 76 times after the diagnosis of Budd–Chiari syndrome and/or portal vein thrombosis; 21 (46%) conceived only once and 24 (53%) conceived twice or more. Patient characteristics were similar in women with Budd–Chiari syndrome and portal vein thrombosis (Table 1). Two women had a history of venous thrombosis before the diagnosis of Budd–Chiari syndrome or portal vein thrombosis, none of the women had previous arterial thrombosis. As standard of care, patients were informed of their individual anticipated risks associated with pregnancy for both mother and fetus, the use of anticoagulation during pregnancy and peripartum management. This included decisions on dose and duration of antepartum and postpartum low-molecular-weight heparin.

Budd–Chiari syndrome

Twelve women had a previous diagnosis of Budd–Chiari syndrome of whom five (42%) also had portal vein thrombosis. The mean ± standard deviation (SD) age at diagnosis was 23 ± 4.6 years, while the mean ± (SD) age at first conception was 31 ± 4.9 years (Table 1). An underlying prothrombotic disorder or oral contraceptive use were the most common risk factors for thrombosis, with more than

Table 1. Patient characteristics

Patient characteristics	All women *n* = 45	Budd–Chiari syndrome* *n* = 12	Portal vein thrombosis *n* = 33
Age at diagnosis (years), mean ± SD	24 ± 7	23 ± 5	25 ± 8
Age at first conception (years), mean ± SD	31 ± 5	31 ± 5	31 ± 5
BMI at first conception (kg/m^2), mean ± SD	24.9 ± 4.1	25.0 ± 3.2	24.8 ± 4.4
Ethnicity, *n* (%)			
African (Sub-Sahara)	2 (4)	1 (8)	1 (3)
Asian	1 (2)	1 (8)	0
Caribbean	2 (4)	1 (8)	1 (3)
Caucasian	30 (67)	5 (42)	25 (76)
Middle Eastern/North African	5 (11)	2 (17)	3 (9)
Aetiology of thrombosis, *n* (%)			
Antiphospholipid syndrome	4 (9)	2 (17)	2 (6)
Inherited thrombophilia	9 (20)	2 (17)	7 (21)
Myeloproliferative neoplasm	7 (16)	1 (8)	6 (18)
Oral contraceptive use	17 (38)	7 (58)	10 (30)
Inflammatory bowel disease	5 (11)	2 (17)	3 (9)
Other**	15 (33)	0	15 (44)
Characteristics at diagnosis, *n* (%)			
Oesophageal varices***	14 (31)	0	14 (42)
Hepatomegaly	9 (20)	7 (58)	2 (6)
Intrahepatic or portosystemic collaterals	18 (40)	6 (50)	12 (36)
Portal hypertension***	38 (84)	12 (100)	26 (79)
Splenomegaly	19 (42)	1 (8)	18 (55)
Treatment before pregnancy, *n* (%)			
Angioplasty hepatic vein	1 (2)	1 (8)	0
Endoscopic variceal ligation	9 (20)	0	9 (27)
Portosystemic shunt (TIPS)	6 (13)	5 (42)	1 (3)
Stenting inferior vena cava	2 (4)	1 (8)	1 (3)
History of pregnancy loss, n (%)			
Early loss (<10 weeks GA)	6 (13)	0	6 (18)
Late loss (≥10 weeks GA)	2 (4)	0	2 (6)
Dose of LMWH during pregnancy			
Prophylactic dose	17 (38)	3 (25)	12 (36)
Therapeutic dose	17 (38)	9 (75)	10 (30)

BMI, body mass index; GA, gestational age; LMWH, low-molecular-weight heparin; SD, standard deviation; TIPS, transjugular intrahepatic portosystemic shunt.
*Five women were diagnosed with Budd–Chiari syndrome and portal vein thrombosis.
**Other risk factors include hyperhomocysteinaemia (*n* = 1), hormonal therapy other than oral contraceptives (*n* = 4), post-surgery (*n* = 4), acute pancreatitis (*n* = 2), malignancy (*n* = 1), umbilical vein catheter (*n* = 2), autoimmune hepatitis (*n* = 1).
***In the portal vein thrombosis cohort, two women developed oesophageal varices before the first pregnancy.

one risk factor being present in 6 of 12 women. None of the women with Budd–Chiari syndrome had oesophageal varices at the start of pregnancy. Imaging studies were not repeated upon pregnancy confirmation. Three women had received a transjugular intrahepatic portosystemic shunt at the time of diagnosis of Budd–Chiari syndrome.

Portal vein thrombosis

Thirty-three women had a previous diagnosis of portal vein thrombosis. The mean ± SD age was 31 ± 5.0 years with a mean ± SD body mass index of 24.8 ± 4.4 kg/m^2 at first conception (Table 1). Antiphospholipid syndrome was present in two women (6%) and secondary to systemic lupus erythematosus in one woman. Seven women (21%) had an inherited thrombophilia and six women (18%) had a myeloproliferative neoplasm. Twenty-six women (77%) had portal hypertension before the first conception and nine women (27%) underwent oesophageal variceal ligation before pregnancy, of whom two were on beta-blockade during pregnancy. Seven women (21%) had a previous pregnancy loss in their medical history, mostly early pregnancy loss.

Table 2. Maternal outcomes

Outcomes	All women		Budd–Chiari syndrome		Portal vein thrombosis	
	All pregnancies* *n* = 75	First pregnancies* *n* = 44	All pregnancies *n* = 19	First pregnancies *n* = 11	All pregnancies* *n* = 56	First pregnancies* *n* = 33
Maternal death, *n* (%)	0	0	0	0	0	0
Gestational course, *n* (%)						
Antepartum vaginal bleeding	1 (1)	1 (2)	1 (5)	1 (9)	0	0
Oesophageal varices in pregnancy	3 (4)	3 (7)	1 (5)	1 (9)	2 (4)	2 (6)
Placental abruption	4 (5)	1 (2)	2 (11)	1 (9)	2 (4)	0
Pre-eclampsia	7 (9)	4 (9)	2 (11)	1 (9)	6 (11)	4 (12)
Pregnancy-induced hypertension	1 (1)	0	0	0	1 (2)	0
Portal hypertension in pregnancy	1 (1)	1 (2)	1 (5)	1 (9)	0	0
Variceal bleeding**	2 (3)	2 (4)	0	0	2 (4)	2 (6)
Thrombotic events, *n* (%)						
Venous thrombosis	1 (1)	0	0	0	1 (2)	0
Arterial thrombosis	1 (1)	0	0	0	1 (2)	0

*One woman with portal vein thrombosis had a twin pregnancy (first pregnancy).
**One woman with portal vein thrombosis had a precautionary intervention, no active variceal bleeding.

Anticoagulant therapy

Before pregnancy, 19 (42%) women used anticoagulant treatment with vitamin K antagonists (17 of 19) or direct oral anticoagulants (2 of 19). During pregnancy, all 12 women with Budd–Chiari syndrome and 73% of women with portal vein thrombosis (24 of 33) used anticoagulant treatment. None of the women used antiplatelet medication before pregnancy. At first pregnancy confirmation, 38 of 45 women (84%) either switched to or started on low-molecular-weight heparin; 17 on a therapeutic dose, 17 on a prophylactic dose, and in four women the dose was unknown. In 7 of 45 (16%) women no anticoagulation was given during pregnancy. Low-molecular-weight heparin was continued throughout pregnancy and in most (30 of 38; 79%) women also in the postpartum period. Standard peripartum management was to stop anticoagulant medication at the start of contractions or have the last dose 24 hours before induction of labour. Anticoagulant therapy was restarted 12–24 hours after birth if postpartum haemostasis was achieved.

Maternal outcome

One woman with Budd–Chiari syndrome was diagnosed with ectopic pregnancy and this pregnancy was excluded from the analyses. No maternal mortality was observed in the 12 women with Budd–Chiari syndrome and none experienced complications related to portal hypertension. One woman with pre-existent portal hypertension was diagnosed with oesophageal varices during pregnancy but she did not experience a bleeding event during the first pregnancy. No thrombotic events occurred during the first pregnancy and one woman (9%) experienced antepartum vaginal bleeding (Table 2). Transjugular intrahepatic portosystemic shunts remained patent in all three patients.

In 33 women with portal vein thrombosis (first pregnancies), no maternal deaths were observed. Two women (6%) with pre-existent oesophageal varices had a variceal bleeding during pregnancy that required intervention; one woman, without adequate beta-blocker prophylaxis before pregnancy, had a variceal bleeding at 22 weeks of gestation and was temporarily admitted to the intensive care unit with good maternal and neonatal outcome. The second woman had received adequate band ligation before pregnancy but nonetheless experienced variceal bleeding during pregnancy, which was quickly controlled by emergent band ligation on the ward (Table 2). Four women (12%) were diagnosed with pre-eclampsia during the first pregnancy.

Presence of portal hypertension ($n = 3$) or oesophageal varices ($n = 2$) before pregnancy was not significantly associated with adverse maternal outcome in the first pregnancy (OR 0.22; 95% CI 0.03–1.66 and OR 1.19; 95% CI 0.18–8.00, respectively) (Table S1). Three subsequent pregnancies were complicated by placental abruption (10%), all leading to emergency caesarean sections with live birth as outcome. Two women had a thrombotic event during a subsequent pregnancy while on prophylactic dose low-molecular-weight heparin; one woman developed pulmonary embolism and one woman suffered from a transient ischaemic attack.

Table 3. Fetal and neonatal outcomes

Outcomes	All women		Budd–Chiari syndrome*		Portal vein thrombosis	
	All pregnancies *n* = 76	First pregnancies *n* = 45	All pregnancies *n* = 19	First pregnancies *n* = 11	All pregnancies *n* = 57	First pregnancies *n* = 34
Pregnancy loss, *n* (%)	22 (29)	11 (24)	8 (42)	5 (45)	14 (25)	6 (18)
Early pregnancy loss (<10 weeks GA)	15 (68)	6 (55)	6 (75)	3 (60)	9 (64)	3 (50)
Late pregnancy loss (10–24 weeks GA)	7 (32)	5 (45)	2 (25)	2 (40)	5 (36)	3 (50)
Neonatal outcomes, *n* (%)**						
Live birth***	54 (71)	34 (76)	11 (58)	6 (55)	43 (75)	28 (82)
Gestational age ≥37 weeks (term live birth)	40 (77)	26 (79)	8 (73)	5 (83)	32 (78)	21 (78)
Gestational age 32–36 weeks	8 (15)	5 (15)	1 (9)	0	7 (17)	5 (18)
Gestational age 24–31 weeks	4 (8)	2 (6)	2 (18)	1 (17)	2 (5)	1 (4)
Mortality						
Perinatal mortality	0	0	0	0	0	0
Death >28 days	1 (2)	0	1 (9)	0	0	0
Birthweight						
SGA <10th centile	12 (22)	9 (26)	6 (55)	3 (50)	6 (14)	6 (21)
SGA<3rd centile	3 (6)	2 (6)	1 (9)	0	2 (5)	2 (7)
Neonatal adverse events						
Apgar <7 (5 min)	2 (4)	2 (6)	1 (9)	1 (17)	1 (2)	1 (4)
pH umbilical cord <7.21	4 (7)	2 (6)	2 (18)	1 (17)	2 (5)	1 (4)
Admission to NICU	8 (15)	5 (15)	3 (27)	1 (17)	5 (12)	4 (14)
IRDS	1 (2)	1 (15)	0	0	1 (2)	1 (4)

GA, gestational age; IRDS, infant respiratory distress syndrome; NICU, neonatal intensive care unit; SGA, small for gestational age.
*One ectopic pregnancy, excluded from analyses.
**Neonatal outcomes presented as proportion of the number of live births per cohort.
***Gestational age unknown for two second pregnancies and one first pregnancy in the portal vein thrombosis cohort.

Live birth

The live birth rate in the first pregnancy was 55% (6 of 11) in women with Budd–Chiari syndrome; 66% (4 of 6) in women with Budd–Chiari syndrome only and 40% (2 of 5) in women with both Budd–Chiari syndrome and portal vein thrombosis. Three (60%) pregnancy losses in the first pregnancy occurred before 10 weeks of gestation (3 of 5; 60%); excluding all first-trimester losses produced a live birth rate of 75% (6 of 8). We observed one fetal death at 21 weeks of gestation due to an intrauterine infection. One neonate died 12 weeks after a very premature delivery at 24 weeks of gestation. Three of six (50%) neonates had a birthweight below the tenth centile; none were below the third centile (Table 3).

In women with portal vein thrombosis, the live birth rate in the first pregnancy was 82% (28 of 34). Three of six pregnancy losses occurred before 10 weeks of gestation and three were late pregnancy losses (all at 11 gestational weeks); if the first-trimester losses were excluded, the live birth rate was 90% (28 of 31). Six of thirty-four neonates had a birthweight below the tenth centile (21%) of whom two had a birthweight below the third centile (2 of 6; 33%) (Table 3).

An analysis based on the association between live birth rate and number of pregnancies (one versus two or more pregnancies), did not demonstrate a significant difference in live birth rate between women with one pregnancy and women with two or more pregnancies; 81% versus 71% (OR 0.57; 95% CI 0.14–2.31). Maternal factors including age and body mass index at conception, underlying prothrombotic disorders or use of anticoagulation in pregnancy were not statistically significantly associated with pregnancy loss in the first pregnancy (Table S2).

Obstetric outcome

Seventeen women delivered vaginally and 14 women underwent a caesarean section, of which 11 were planned (79%) and three were unplanned or emergency caesarean sections (21%). In the majority of planned caesarean sections, the indication was maternal, as the bleeding risk was considered too high to deliver vaginally. Most women with Budd–Chiari syndrome had uncomplicated vaginal deliveries in the first pregnancy (73%). Half of the women with portal vein thrombosis (13 of 26) had vaginal deliveries. The other half (13 of 26) had planned caesarean sections

Table 4. Obstetric outcomes

Obstetric outcomes	All women		Budd–Chiari syndrome		Portal vein thrombosis	
	All pregnancies *n* = 54	First pregnancies *n* = 34	All pregnancies *n* = 11	First pregnancies *n* = 6	All pregnancies *n* = 43	First pregnancies *n* = 28
Postpartum blood loss, *n* (%)						
0–500 mL	22 (41)	13 (38)	2 (18)	1 (17)	20 (47)	12 (43)
500–1000 mL	10 (19)	6 (18)	1 (9)	0	9 (21)	6 (21)
>1000 mL	8 (15)	6 (18)	1 (9)	1 (17)	7 (16)	5 (18)
Mode of delivery*, *n* (%)						
Vaginal	25 (46)	17 (50)	8 (73)	4 (67)	17 (40)	13 (46)
Spontaneous onset of labour	15 (60)	16 (94)	7 (88)	3 (75)	8 (47)	13 (100)
Induction of labour	8 (32)	0	0	0	8 (47)	0
Vacuum extraction	2 (8)	1 (6)	1 (12)	1 (25)	1 (6)	0
Caesarean	22 (41)	14 (42)	1 (9)	1 (17)	21 (49)	13 (46)
Primary	18 (82)	11 (79)	0	0	18 (86)	11 (85)
Emergency	4 (18)	3 (21)	1 (100)	1 (100)	3 (14)	2 (15)
Placental delivery, *n* (%)						
Spontaneous	22 (41)	13 (38)	8 (73)	4 (67)	14 (33)	9 (32)
Manual	2 (4)	2 (6)	0	0	2 (5)	2 (7)

*Mode of delivery unknown in two women with Budd–Chiari syndrome and in four women with portal vein thrombosis.

(85%). Twelve neonates were born small for gestational age (24%) of whom three (6%) had a birthweight below the third centile (Table 4).

The median reported amount of postpartum blood loss was 400 ml, ranging from 100 ml to 4000 ml. Of the six women who experienced postpartum bleeding of more than 1000 ml in the first pregnancy, 50% (3 of 6) occurred after vaginal delivery. Interventions included red blood cell transfusion and administration of tranexamic acid. Four of these six women (67%) were on anticoagulant treatment shortly before delivery.

Discussion

Budd–Chiari syndrome and portal vein thrombosis are rare disorders, particularly in women of reproductive age.[4,16] We here report detailed data on management and maternal, neonatal and obstetric outcomes of pregnancy in this patient population. In our multicentre retrospective cohort study on pregnancy outcomes in 12 women with Budd–Chiari syndrome and 33 with portal vein thrombosis, we observed live birth in 76% of first pregnancies. There was no maternal mortality and the risk of maternal thrombotic and bleeding events was lower than expected. Pregnancy outcomes did not differ between women with concomitant portal hypertension and those without. Anticoagulation during pregnancy was not associated with an increased risk of pregnancy loss or maternal adverse events.

Underlying prothrombotic conditions were identified in almost all women with Budd–Chiari syndrome and portal vein thrombosis, which is in line with the up to 90% reported in previous studies.[4,11,21,22] Prophylactic or therapeutic doses of low-molecular-weight heparin during pregnancy and the postpartum period were given in all the women with Budd–Chiari syndrome and in the majority of women with portal vein thrombosis. Venous thrombosis, most notably pulmonary embolism, remains one of the leading causes of maternal morbidity during pregnancy in general, with an incidence of pregnancy-related venous thromboembolism ranging from 1 to 2 per 1000 deliveries.[23,24] The risk of recurrent venous thromboembolism is three- to four-fold higher during a subsequent pregnancy, with absolute risk estimated to be up to 10% without thromboprophylaxis.[25,26] Histories of thrombosis and thrombophilia are well-recognized factors contributing to the significantly higher risk of venous thromboembolism during pregnancy.[27,28] However, we observed a very low rate of recurrent thrombosis and bleeding in our cohort, suggesting that the use of anticoagulation in this specific population with often underlying prothrombotic disease is effective and safe in the prevention of pregnancy-related recurrent venous thromboembolism.[29] The fact that some women with portal vein thrombosis were not on anticoagulant therapy either before or during pregnancy would suggest that they were deemed to have been at very low risk of recurrence. This may have influenced the overall favourable outcomes.

Although the observed number of term live births was higher than expected based on previous studies, the risk of pregnancy loss was substantial and five patients could not conceive at all despite trying. Both inherited and acquired thrombophilia have been associated with adverse pregnancy outcomes.[30] Subgroup differences between Budd–Chiari syndrome and portal vein thrombosis probably exist, but whether they are relevant to the course and outcome of pregnancy remains unclear. Considering the relatively small study population, further analysis based on aetiological factors was deemed not feasible. Although antithrombotic treatment is given to prevent recurrent thrombosis during pregnancy, there may be additional beneficial effects on pregnancy outcome.[31–33]

No perinatal mortality was observed and most neonates were born at term. A birthweight below the tenth centile was used as a proxy for fetal growth restriction in the absence of information on functional placental markers such as Doppler measurements. Twelve neonates were born small for gestational age (24%) of whom three (6%) had a birthweight below the third centile. Other placenta-mediated outcomes, such as placental abruption and pre-eclampsia, occurred in 11% of neonates. Although these numbers are small, it is plausible that Budd–Chiari syndrome and portal vein thrombosis are associated with a higher risk of placental insufficiency and associated adverse neonatal outcomes. Hypothetically, similar to reduced maternal cardiac diastolic function, venous return pressure may be higher, resulting in poor placentation and an affect on pregnancy outcome.[34]

We observed a relatively low rate of variceal bleeding (3%) during pregnancy and only in women with pre-existent oesophageal varices, particularly given that the vast majority of women used anticoagulation therapy during pregnancy (albeit 17/38 at a prophylactic dose). Previous studies have suggested that variceal bleeding occurs in up to 15% of pregnancies in this population, but results from these small cohort studies are conflicting.[16,34,35] Approximately half of the women in our cohort delivered vaginally. This is in line with two previous studies on pregnancy outcomes in women with Budd–Chiari syndrome, in which 47–70% of women had a caesarean section.[12,13] Presence of oesophageal varices is a relative contraindication for vaginal delivery as high intra-abdominal pressure during uterine contractions in the first and second stages of labour may induce oesophageal variceal bleeding. In high-risk women, this would justify choosing a caesarean section upfront. Overall, the mode of delivery did not affect the risk of postpartum bleeding. This is in line with more recent cohort studies, which suggest that if there is no clinically significant variceal bleeding risk then there is no specific need for a caesarean section and a medically assisted vaginal delivery is still the preferred mode.[10,12]

In addition to clinical outcomes, we aimed to evaluate practice regarding (pre)pregnancy counselling of women with Budd–Chiari syndrome or portal vein thrombosis. Of all women with a diagnosis of Budd–Chiari syndrome potentially eligible for study participation, we identified 11 who were advised against pregnancy and one who was advised to actively terminate pregnancy because the risk of oesophageal bleeding was considered too high. In general, Budd–Chiari syndrome or portal vein thrombosis is not considered a clear contraindication for pregnancy. Treating physicians at all sites opted for a multidisciplinary approach and the individual patients were carefully counselled before pregnancy. These results reflect current clinical practice in four academic centres in The Netherlands and may differ in other countries.

The small sample size, the observational and retrospective nature of our study, and heterogeneity in the study population are limitations for interpreting our results. These are, however, in line with other retrospective small studies, with similar limitations, on pregnancy outcome in this population.[12,13,16,35,36] Additionally, selection bias should be considered as some women may have failed to conceive and women with the highest risk of adverse pregnancy outcome may have been negatively counselled and refrained from pregnancy.

However, as counselling may differ in individual cases, both with respect to the message of the treating physician and its reception by the patient, our cohort probably still includes women considered to be high risk by some. Taking into account the sparsity of data on this particular topic, the results from our study are relevant for clinical practice and may provide evidence for guidance, particularly with regard to counselling for pregnancy.

The high number of term live births and the lower than expected rate of pregnancy-related maternal and fetal morbidity in our small cohort indicate that there is no absolute contraindication for pregnancy in patients with Budd–Chiari syndrome and/or portal vein thrombosis. A multidisciplinary approach is indispensable to increase the chances of a favourable pregnancy outcome for both mother and child taking into account comorbidities.

Disclosure of interests

MNL reports grants from GSK and Aspen, personal fees from BMS Pfizer and non-financial support from Novo Nordisk; all outside the scope of the submitted work. All other authors have nothing to disclose. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

HMW, ENH, SED, SM and WG participated in all aspects of the study and authored the manuscript. HMW, ENH and JRD

retrieved patient data. All authors interpreted data, reviewed drafts and approved the final draft of the manuscript.

Details of ethics approval

The Medical Ethics Committee of the Amsterdam UMC deemed that the Medical Research involving Human Subjects Act (WMO) did not apply to this study (W19_456) and official approval was not required.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. Association between patient characteristics and maternal outcome (any adverse event) for the first pregnancy.

Table S2. Association between patient characteristics and fetal outcome for the first pregnancy. ■

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