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# Portal Vein Thrombosis Experiences in a Tertiary Neonatal Intensive Care Unit

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The preliminary results of this article were presented at the 7th UTSAK (28/29 August, 2021) Congress with patients diagnosed with PVT between January 2017 and January 2020.

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## *Abstract*

**Objective:** The aim of the study was to present the clinical and descriptive features of patients with portal vein thrombosis.

**Methods:** The study was conducted in a tertiary neonatal intensive care unit in Istanbul, Turkey. We included the patients diagnosed with portal vein thrombosis hospitalized in our neonatal intensive care unit between January 2017 and December 2021, retrospectively. We investigated the birth history, anthropometric measurements, the postnatal day of portal vein thrombosis detected, and clinical history.

**Results:** Nineteen patients (12 male) were eligible for the study. Portal vein thrombosis incidence was 3.9 per 1000 infants admitted to our neonatal intensive care unit. The mean gestational week was 35.1 ± 4.8 weeks. The median birth weight was 2835 g (1335-3250), and the median length was 47 cm (38-50). We detected portal vein thrombosis on median postnatal 13 days. Portal vein thrombosis was in the left portal vein in 84.2% (n = 16) and the main portal vein in 15.8% (n = 3) patients. About 68.4% (n = 12) of the patients had umbilical venous catheter, 47.4% (n = 9) had a history of perinatal asphyxia, 26.3% (n = 5) had necrotizing enterocolitis, 5.3% (n = 1) had tracheoesophageal fistula + anal atresia, and 5.3% (n = 1) had an omphalocele. In 15.7% (n = 3) of the patients, we detected portal vein thrombosis without any known clinical risk factor on the first postnatal day. About 26.3% (n = 5) of patients underwent anticoagulation treatment. All the thrombosis was re-canalized, except 1 patient.

**Conclusion:** Portal vein thrombosis can be seen on the first postnatal day, even in babies with no perinatal problems. The cases had asphyxia and intra-abdominal operation/necrotizing enterocolitis as risk factors. Portal vein thrombosis incidence was 3.9 per 1000 neonatal intensive care unit admission.

**Keywords:** Neonatal portal vein thrombosis, perinatal asphyxia, necrotizing enterocolitis

## Introduction

An umbilical venous catheter (UVC) or other central catheters may be required in patients treated in the neonatal intensive care unit (NICU). However, these may cause catheter-related infections and thrombosis by disrupting the hemostatic balance of newborn babies.[1,2] The properties of the fibrinolytic system and coagulation factors tend to develop thrombosis in newborns due to triggering factors such as indwelling catheters.[3] Portal vein thrombosis in the neonatal period is seen in 3.5 patients per 1000 newborns in NICUs.[4]

The etiology of neonatal extrahepatic portal vein thrombosis (PVT) (will be mentioned as PVT) is multifactorial and separated as maternal, neonatal, and catheter-related risk factors.[1] Maternal risk factors are maternal diabetes mellitus, infection, preeclampsia, dyslipidemia, metabolic syndrome, anti-phospholipid antibody syndrome, emergency cesarean delivery, prolonged premature rupture of membranes, and hereditary thrombophilia. Neonatal risk factors for the development of PVT are sepsis, need for mechanical ventilation, perinatal asphyxia, polycythemia, congenital heart disease, and dehydration. Furthermore, central venous catheter-related risk factors are low birth weight, prematurity, using the catheter for more than 6 days, improper placement of the UVC, blood product transfusion from UVC, mechanical ventilation, and history of surgery.[1]

Portal vein thrombosis is associated with UVC,[1,5] and there is often a history of UVC in the etiology; even in autopsy series, portal vein thrombus was found in 20%-40% of infants who underwent umbilical venous catheterization.[5]

Doppler ultrasound imaging reveals PVT in an easy and non-invasive way in most cases. Contrast angiography is considered the gold standard; however, its width of usage in clinics is not broad due to its invasive nature.[6]

The benefit of anticoagulation in neonatal PVT is uncertain as most cases resolve and re-canalize without intervention. Therefore, supportive care, follow-up, and conservative management will be enough and recommended for most neonates with PVT limited to the left portal vein. If the thrombus extends into the main portal vein, anticoagulant therapy should be initiated with low-molecule-weight heparin.[5]

As thrombophilia mutations may be detected in some cases,[2] risk factors in the development of neonatal extrahepatic PVT that occur during the clinical course of the infants are more prominent than hereditary thrombophilic factors.[1] Therefore, further thrombosis research is not needed in routine clinical practice.[1]

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In this study, we present the PVT-diagnosed cases that had undergone intra-abdominal surgery, were detected incidentally without predisposition, and had perinatal asphyxia -which we believe to be a reason for our higher PVT rate in our NICU.

## Methods

We included all patients diagnosed with a PVT and treated at the NICUs of Güngören Hospital between January 2017 and December 2021, retrospectively.

We recorded catheter use, anthropometric measurements (height, weight, and head circumference), birth history, postnatal day of PVT detected, and survival status. Also, we recorded the possible risk factors:

1. Maternal risk factors (maternal diabetes mellitus, infection, preeclampsia, metabolic syndrome, phospholipid antibody syndrome, emergency cesarean delivery, prolonged premature rupture of membranes, and hereditary thrombophilia).[1]
2. Neonatal risk factors (presence of sepsis, mechanical ventilation, perinatal asphyxia, polycythemia, congenital heart disease, dehydration, intra-abdominal operation, necrotizing enterocolitis, and hemolysis).[1,7,8]
3. Catheter-related risk factors.[1]

We could not obtain detailed maternal risk factors about phospholipid antibody syndrome and hereditary thrombophilia due to lack of data.

The ethical committee approval was obtained from the İstanbul University-Cerrahpaşa University (Date: June 30, 2022, Number: 409331).

## Statistics

We used the Mann–Whitney *U*-test to compare 2 groups with continuous variables with skewed distribution and Fisher's exact test to compare categorical data. Type 1 error <0.05 was considered statistically significant. We used Jamovi 2.2.5 statistical package program for statistical calculations.

## Results

A total of 4910 patients were treated in our NICU. Nineteen patients (12 boys and 7 girls) were eligible for the study. The incidence of PVT was 3.9 per 1000 NICU admissions.

Anthropometric data and birth histories of the patients are presented in Table 1.

The clinical characteristics and concomitant factors of PVT are presented in Table 2.

**Table 1.** Anthropometric Data and Birth History of the Patients and Postnatal Day of Diagnosis

| | |
|---|---|
| Delivery type, % | 68.4% cesarean section, 31.6% normal spontaneous vaginal delivery |
| Gestational age, mean ± SD | 35.1 ± 4.8 |
| Birth weight, median (IQR) | 2835 (1335-3250) |
| Postnatal diagnosis day in term newborns, median (IQR) | 13 (0-18) |
| Postnatal diagnosis day in preterm newborns, median (IQR) | 14 (8-22.8) |

IQR, interquartile range.

**Table 2.** Clinical Characteristics and Concomitant Factors of Portal Vein Thrombosis

| | |
|---|---|
| Thrombosis detection, median (IQR) | 13 (6-19) days |
| Preterm/term | 10/9 |
| Location, % (n) | Left portal vein: 84.2% (n = 16)<br>Main portal vein:15.8% (n = 3) |
| Maternal risk factors | |
| Maternal DM | 0% |
| Infection | 10.5% (n = 2) |
| Preeclampsia | 15.8% (n = 3) |
| Metabolic syndrome | 5.3% (n = 1) |
| Emergency cesarean delivery | 36.8% (n = 7) |
| Prolonged premature rupture of membranes | 5.3% (n = 1) |
| Neonatal risk factors | |
| SGA | 15.9% (n = 3) |
| Presence of sepsis | 21.1% (n = 4) |
| Mechanical ventilation | 52.6% (n = 10) |
| Perinatal asphyxia, % (n) | 47.4% (n = 9)<br>Mild (n = 6)<br>Moderate (n = 2)<br>Severe (n = 1) |
| Polycythemia | 0% |
| Congenital heart disease | 5.3% (n = 1) |
| Dehydration | 0% |
| Intra-abdominal operation | 10.5% (n = 2) |
| Necrotizing enterocolitis | 31.6% (n = 6) |
| Hemolysis | 10.5% (n = 2) |
| Catheter-related risk factors | |
| Umbilical venous catheterization, % (n) | 68.4% (n = 13) |
| Others | |
| No accompanying medical factors with the infant | 15.8% (n = 3) |
| Undergone treatment | 26.3% (n = 5) |

Perinatal asphyxia sub-characteristics are presented according to Sarnat & Sarnat classification.[9]
DM, diabetes mellitus; IQR, interquartile range; SGA, small-for-gestational age.

There was no statistically significant difference between preterm and term babies on the day of diagnosis (Mann–Whitney *U*-test; $P = .305$).

The thrombus was located in the left portal vein in 80% of preterm infants and the main portal vein in 20% of the preterm infants, while the thrombus was located in the left portal vein in 89% and the main portal vein in 11% of the term infants. There

was no statistically significant difference between preterm and term babies for thrombus location. About 12.6% had an abdominal surgery history (tracheoesophageal fistula + anal atresia and omphalocele).

There were no accompanying factors in 15.8% (n = 3) of the patients diagnosed on their first day of life; thus, none needed anticoagulant therapy. However, we started low-molecular-weight heparin in 5 patients with portal hypertension, hepatosplenomegaly, or progressive thrombosis.

We started anticoagulants in 5 patients; thus, the 2 patients were symptomatic, and their thrombosis was in the main portal vein, and the other 3 patients had progression on their thrombus in the left portal vein. All patients' portal veins were re-canalized except 1 patient who was discharged and was given low-molecule-weight heparin therapy as an outpatient treatment.

We revealed PVT in 3 patients in our study on the day of birth without any neonatal or catheter-related risk factors. These patients had maternal risk factors such as preeclampsia, gestational diabetes, and prolonged premature rupture of membranes in their prenatal histories.

## Discussion

Portal vein thrombosis is a rare disease in NICUs. It is reported that its incidence is 2.5 per 1000 infants admitted to the NICU.[10] However, PVT rate was 3.9 per 1000 NICU admissions in our study. We could not explain this unexpected difference scientifically. But we think that neonatal surgery and perinatal asphyxia cases increased the incidence of PVT in our patient group, which resulted in a difference between our results and the literature data.

There is male dominance in VT cases, and it is reported between 52.3% and 60% in the literature.[2,10-13] Beyond it being more common in boys, some studies have identified male gender as a risk factor for the development of PVT.[14] Our patient group consisted of male infants with a rate of 63.2% in our patient group, which is consistent with the literature.

As we review the literature, PVT is more common in preterm babies. While PVT was reported to be 1.47 to 1.57 times more common in preterm babies than in term babies,[10,11,15] another study reported this rate to be 0.79.[13] Even a study defined prematurity as a risk factor for PVT.[1] In our study, 52.6% of the patients had a history of preterm birth. The presence of a central catheter is indirectly associated with a higher overall rate of neonatal thrombosis in prematurity.[14]

As we assess the day of postnatal diagnosis, a study reported the postnatal diagnosis day to be 15.9 ± 26.89 days in preterm babies, 12.8 ± 19.4 days in term infants, and 14.6 ± 24 days in all babies.[15] In our study, the median age at diagnosis was 14 days in preterm infants and 13 days in term infants. There was no statistically significant difference between preterm and term babies on postnatal diagnosis day ($P = .305$).

As we approach PVT in terms of the location of the thrombus, in 1 study, 93.2% of the preterm babies and 90% of the term babies had thrombus in the left portal vein, while 10% of the term babies and 4.5% of the preterm babies had thrombus in the main portal vein. Also, 2.3% of preterm babies had thrombus in the right portal vein.[15] None of the patients had a thrombus in the right portal vein in our study group. While 80% of preterm infants had a thrombus in the left portal vein and 20% in the main portal vein, 89% of the term infants had a thrombus in the left portal vein, and 11% had 1 in the main portal vein in our patient group.

Among the risk factors for PVT, umbilical catheterization is one of the leading risk factors.[1,11,14,15] A study reported that 54.5% of preterm babies and 73.3% of term babies had umbilical vein catheters.[15] In our study, 55.5% of term infants, 80% of preterm infants, and 68.4% of all patients had a UVC.

The history of major surgery in newborns is a defined risk factor among the neonatal risk factors for PVT.[1,7] A study reported that 9.5% of the patients had a history of intra-abdominal surgery.[13] Consistent with the literature, 10.6% of our patients had a history of intra-abdominal surgery who underwent the operation for anal atresia and omphalocele.

Perinatal asphyxia is also a risk factor among defined risk factors in the neonatal period.[2,7,8,13-15] In a study including patients with thromboembolism, the perinatal asphyxia rate was 2.5%. The perinatal asphyxia rate was 47.4% among our PVT study group. We think that as our NICU is a referral center for perinatal asphyxia patients, this rate was higher.

The treatment algorithm is not affected by hereditary thrombophilia presence of neonatal extrahepatic PVT. Therefore, genetic thrombophilia investigation tests are not routine in the neonatal period.[1] We detected PVT on the first postnatal day without any clinical problem in 1 of our term patients, and we searched further with thrombophilia tests which revealed decreased protein C and protein S levels and antithrombin III activities. However, in a publication researching hereditary causes, thrombophilia mutations were found in half of the PVT cases. The study reported heterozygous factor 5 mutations, homozygous Methylenetetrahydrof olate reductase (MTHFR) gene mutation, and homozygous/hete rozygous plasminogen activator inhibitor type 1 mutation.[2] Thus, another publication revealed that 8.3% of patients had genetic mutations, antithrombin-3 deficiency, and factor 5 Leiden mutation.[10] According to the data in our study and these studies,[2,10] genetic factors do not affect the clinical judgment, so the necessity of thrombophilia panel research in thrombosis diagnosed-patients debates.

In addition, there are significant risk factors (hereditary thrombophilia and phospholipid antibody syndrome) reported in the references[1] that we could not use due to lack of data.

## Conclusion

Portal vein thrombosis can be seen on the first postnatal day due to maternal reasons, even in babies who do not suffer from perinatal problems. In our case series, UVC, asphyxia, and history of intra-abdominal operation constituted most of the cases. Supportive care, follow-up, and conservative management were enough for these patients, but only a quarter needed anticoagulant therapy. Routine thrombophilia panel tests did not change the treatment course.

Additionally, the PVT rate was 3.9 per 1000 patients in our third-level NICU.

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