Van Med J 33 (1):31 -39, 2026
DOI: 10.5505/vmj.2026.42275

Intrauterine Transfusion for Parvovirus B19–Related Fetal Anemia: A Comparative Cohort Study of Hydropic and Non-Hydropic Outcomes

Ruken Dayanan, Dilara Duygulu Bulan, Merve Ayas Ozkan, Betul Tokgoz Cakir, Sevki Celen

Etlik City Hospital, Department of Perinatology, Ankara, Türkiye

Abstract

Introduction: To evaluate the efficacy and safety of intrauterine transfusion (IUT) in fetuses with parvovirus B19–related anemia, and to compare prenatal, procedural, and neonatal outcomes between hydropic and non-hydropic presentations.

Materials and Methods: This retrospective cohort included 41 pregnancies with confirmed fetal parvovirus B19 infection managed between December 2022 and December 2024 in Department of perinatology Ankara Etlik City Hospital. Fetuses were stratified based on the presence of hydrops. MCA Doppler values, transfusion parameters, hematologic response, and perinatal outcomes were compared between hydropic (n=29) and non-hydropic (n=12) groups.

Results: IUT was performed in 18 fetuses (14 hydropic, 4 non-hydropic). The median gestational age at first IUT was 26 weeks in hydropic and 27 weeks in non-hydropic cases. Pre-transfusion hemoglobin was significantly lower in hydropic fetuses (4.7 vs. 8.2 g/dL), while post-transfusion levels did not differ significantly. MCA-PSV values were significantly higher in hydropic cases (median 1.67 vs. 1.35 MoM) and showed significant improvement following transfusion. Fetal pH values increased after IUT, although this change was not statistically significant. No procedure-related fetal deaths occurred. Minor complications were observed in 21.4% of hydropic and 25% of non-hydropic fetuses. Live birth was significantly less frequent in hydropic fetuses (48.2% vs. 83.3%), and perinatal mortality was higher (37.9% vs. 16.7%).

Conclusion: Intrauterine transfusion is a safe and effective treatment for parvovirus B19–related fetal anemia. Although hydropic fetuses remain at elevated risk, timely transfusion—guided by MCA Doppler surveillance—can significantly improve survival and reduce perinatal morbidity.

Key words: Parvovirus B19; anemia; fetal; blood transfusion; intrauterine; hydrops fetalis; ultrasonography, doppler; prenatal treatment.

Introduction

Parvovirus B19 (B19V) is a small, non-enveloped DNA virus that commonly causes erythema infectiosum (fifth disease) in children. However, when contracted during pregnancy, it can lead to serious fetal complications including anemia, hydrops fetalis, miscarriage, and intrauterine fetal demise (IUFD) (1). Approximately one-third of pregnant women are non-immune to B19V, and seroconversion rates of 1–2% per year have been reported in endemic settings, rising further during epidemics (2). While maternal infection is typically asymptomatic or mild, vertical transmission occurs in 30–50% of cases (3). While most fetal infections are subclinical or self-limiting, a subset progresses to significant complications such as severe fetal anemia, hydrops fetalis, or even miscarriage and intrauterine fetal demise (IUFD), particularly when infection occurs during the first half of gestation (4). Hydrops fetalis, characterized by pathological fluid accumulation in fetal compartments, is one of the most severe consequences of congenital B19V infection. The virus demonstrates a tropism for erythroid progenitor cells in the fetal liver and bone marrow, leading to red cell aplasia and profound anemia (5,6). The resultant high-output cardiac failure, often exacerbated by viral myocardial involvement, leads to the development of hydrops (7). Although the overall incidence of hydrops in B19V-affected pregnancies is relatively low, the risk is substantially higher with earlier gestational infections and is strongly associated with adverse perinatal outcomes if left untreated. Advances in fetal therapy, particularly intrauterine transfusion (IUT), have significantly improved survival in affected fetuses, raising survival rates from 30–50% to as high as 67–84% when administered promptly (4). Despite this, prognosis remains guarded in cases of advanced hydrops due to irreversible cardiac compromise or multiorgan

*Corresponding Author: Ruken Dayanan Department of Perinatology, Ankara Etlik City Hospital, Ankara, Turkey, 06170, Ankara/Turkey
E- mail: rukendayanan@gmail.com
Orcid: Ruken Dayanan 0000-0002-8192-8841, Dilara Duygulu Bulan 0000-0001-9983-2306, Merve Ayas Ozkan 0000-0002-2437-9719, Betul Tokgoz Cakir 0000-0003-0202-4981, Sevki Celen 0000-0001-7033-3474

Received: 24.09.2025, Accepted: 14.11.2025

dysfunction (8). While non-hydropic fetuses often recover with close monitoring alone, hydropic fetuses constitute a high-risk subgroup requiring more aggressive intervention and carrying worse perinatal outcomes (9). However, comparative data focusing on maternal, sonographic, and neonatal differences between hydropic and non-hydropic fetuses in parvovirus B19 infection remain limited. To address this gap, we conducted a retrospective cohort study comparing clinical characteristics, intrauterine transfusion parameters, and neonatal outcomes between these two groups.

Material and Methods

This retrospective cohort study was conducted at the Department of Perinatology, Ankara Etlik City Hospital—a tertiary referral center—between December 2022 and December 2024. A total of 41 pregnant women diagnosed with intrauterine parvovirus B19 infection were included. Cases were identified through systematic review of the hospital electronic medical record system and perinatal diagnostic database, and all pregnancies with laboratory-confirmed maternal parvovirus B19 infection within the study period were eligible. The study was conducted in accordance with the Declaration of Helsinki, with approval from the Ankara Etlik City Hospital Ethics Committee (approval number: AESH-BADEK2–2025-027). Diagnosis of maternal parvovirus B19 infection was established based on clinical suspicion and laboratory confirmation. Specifically, all cases had evidence of recent maternal infection demonstrated by either the presence of serum anti-parvovirus B19 IgM antibodies detected using enzyme-linked immunosorbent assay (ELISA), and/or detection of parvovirus B19 DNA via real-time polymerase chain reaction (PCR) in maternal serum or amniotic fluid samples. In selected cases where serological results were inconclusive or discordant with clinical findings, diagnosis was supported by characteristic fetal sonographic features—such as ascites, skin edema, cardiomegaly, or elevated middle cerebral artery peak systolic velocity (MCA-PSV >1.5 MoM)—with confirmatory PCR testing from amniotic fluid or fetal blood when feasible. Patients were stratified into two groups based on the presence or absence of fetal hydrops at the time of diagnosis: the hydropic group (n=29, 70.7%) and the non-hydropic group (n=12, 29.3%). Hydrops fetalis was defined as abnormal fluid accumulation in at least two fetal compartments (ascites, skin edema, pleural and/or pericardial effusion) on ultrasound. Among the hydropic group, four pregnancies (13.7%) resulted in miscarriage before 20 weeks of gestation and were included in the overall clinical analysis but excluded from neonatal outcome comparisons.

Maternal demographic and obstetric characteristics (age, gravidity, parity, BMI), clinical symptoms (fever, rash, arthralgia), and gestational age at infection were recorded. Ultrasound findings (presence of ascites, pleural/pericardial effusion, skin edema, placentomegaly, cardiomegaly, ventriculomegaly, polyhydramnios) and fetal Doppler parameters, including MCA-PSV and multiples of the median (MoM), were documented at the time of diagnosis. IUT was performed in eligible cases with sonographic and Doppler evidence of fetal anemia, under sterile conditions and continuous real-time ultrasound guidance at a tertiary referral fetal medicine center. Indications for transfusion included Doppler evidence of fetal anemia, defined as a middle cerebral artery peak systolic velocity (MCA-PSV) exceeding 1.5 MoM, and/or the presence of hydrops fetalis on ultrasound. Following local maternal anesthesia, a 20-gauge needle was inserted transabdominally into the umbilical vein at its placental insertion site to achieve intravascular access. Fetal sedation or neuromuscular blockade was not administered. Cordocentesis was performed prior to transfusion to determine baseline hemoglobin, hematocrit, pH, and platelet levels. The transfused blood consisted of type O, RhD-negative packed red blood cells that were irradiated, leukocyte-depleted, cytomegalovirus (CMV)-seronegative, and crossmatched with maternal serum. The transfusion volume was calculated using the following formula: Volume (mL) = [(Target Hct – Fetal Hct) / Donor Hct] × Fetoplacental Blood Volume, where the target hematocrit was 40–50%, the donor hematocrit was ~75–80%, and fetoplacental blood volume was estimated using 0.14 mL per gram of fetal weight (equivalent to 110–150 mL/kg). The transfusion was administered over 10–15 minutes under continuous fetal heart rate monitoring. Post-transfusion, a repeat fetal blood sample was obtained to confirm hematologic response, and follow-up assessment with ultrasound and MCA Doppler was performed within 24–48 hours. Minor and major complications were prospectively recorded. Minor complications included transient fetal bradycardia and needle site bleeding, while major complications were defined as fetal demise within 48 hours post-procedure. No major adverse events occurred. Additional data collected

Table 1: Clinical Comparison of Hydropic vs. Non-Hydropic Fetuses in Parvovirus B19 Infection

	Hydropic fetuses n:29 (70.7%)	Non-hydropic fetuses n:12 (29.3%)	p value
Maternal age (year)	30 (25.5-34.5)	28 (27.0-28.5)	0.021
Gravidity	1 (1-2)	2 (1-3)	0.004
Parity	0 (0-1)	1 (1-2)	0.030
Nulliparous	17 (58.6%)	2 (16.7)	0.019
BMI (kg/m^2)	27.2 (22.3-32.0)	28.4 (24.7-32.0)	0.388
Gestational age at infection (week)	26 (20–29)	21(19-24)	0.119
Maternal Symptoms			
Fever	7 (24.1%)	2 (16.7%)	0.708
Skin Rash	4 (13.8%)	3 (25%)	0.363
Arthralgia	6 (20.7%)	1 (8.3%)	0.407
USG Findings			
Ascites	25 (86.2%)	7 (77.8%)	0.049
Pulmonary Effusion	19 (65.5%)	3 (25.0%)	0.014
Pericardial Effusion	25 (86.2%)	1 (8.3%)	0.001
Skin Edema	22 (75.9%)	0 (0.0%)	0.001
Placentamegaly	16 (55.1%)	2 (16.6%)	0.022
Cardiomegaly	11 (37.9%)	0 (0.0%)	0.018
Ventriculomegaly	2 (6.9%)	0 (0.0%)	0.351
Polihidroamnios	11 (37.9%)	2 (16.6%)	0.174
MCA PSV	60.0 (45.0-71,1)	38.0 (35.2-49.5)	0.002
MCA PSV (MoM)	1.67 (1.35-2.23)	1.35 (1.22-1.72)	0.049
Miscarriage (< 20 weeks)	4 (13.7%)	0 (0.0%)	0.302
Live Birth	14 (48.2%)	10 (83.3)	0.044
Perinatal death	11 (37.9%)	2 (16.7%)	0.047
Intrauterine death	7 (24.1%)	2 (16.7%)	0.708
Neonatal death	4 (13.7%)	0 (0.0%)	0.555
Spontaneous resolution of the infection	3 (12%)	6 (50.0%)	0.036
Need for intrauterine transfusion	16 (64.0%)	4 (33.3%)	0.081
Intrauterine transfusion cases	14 (56.0%)	4 (33.3%)	0.471

Data are expressed as median (Q_1–Q_3) for continuous variables and number (percentage) for categorical variables. p-values were calculated using the Student's t-test or Mann–Whitney U test for continuous variables, and Pearson's chi-square test or Fisher's exact test for categorical variables BMI: Body Mass Index; MCA PSV: Middle Cerebral Artery Peak Systolic Velocity; MoM: Multiples of the Median; USG: Ultrasonography; IUT: Intrauterine Transfusion.

included gestational age at IUT, time interval between maternal diagnosis and first IUT, transfused volume, number of IUTs, and post-transfusion hematologic parameters. Delivery outcomes encompassed gestational age at birth, mode of delivery, birth weight, Apgar scores, umbilical cord pH, fetal hemoglobin and hematocrit, neonatal anemia and thrombocytopenia, need for postnatal transfusion, NICU admission, respiratory complications, cranial imaging findings, and PCR-confirmed neonatal parvovirus B19 positivity. Comparative analyses were conducted between the hydropic and non-hydropic groups for all variables.

Ethical Approval: Approval was obtained from the Institutional Review Board of Ankara Etlik City Hospital (approval number: AESH-BADEK2–2025-027). In this study, due to its retrospective nature, informed consent was waived with the approval of the Ethics Committee of Ankara Etlik City Hospital. All data were anonymized, and participant confidentiality was

strictly maintained. This research was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Statistical Analysis: All statistical analyses were performed under the supervision of a biostatistics expert using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA). The normality of distribution for continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous variables were presented as mean ± standard deviation (SD) for normally distributed data or as median with interquartile range (Q1–Q3) for non-normally distributed data. For comparisons between hydropic and non-hydropic groups, the Student's t-test was used for normally distributed continuous variables, and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. A p-value < 0.05 was considered statistically significant. Additionally, a post-hoc power analysis demonstrated that the study had a power of 0.82 at an alpha level of 0.05 for detecting the observed difference in live birth rate between hydropic and non-hydropic groups, confirming adequate power for the primary outcome despite the limited sample size."

Table 2: Intrauterine Transfusion Characteristics in Hydropic vs. Non-Hydropic Fetuses with Parvovirus B19 Infection

	Hydropic fetuses n:14 (77.7%)	Non-hydropic fetuses n:4 (22.3%)	p value
Gestational age at IUT (week)	26 (24.0-28.5)	27 (26.5-28.0)	0.513
Hemoglobin before IUT (g/dL)	4.7 (3.9-6.4)	8.2 (7.6-8.7)	0.010
Hemoglobin after IUT (g/dL)	9.8 (9.1-12.0)	11.2 (11.0-11.7)	0.670
pH before IUT	7.21 (7.11-7.30)	7.24 (7.11-7.32)	0.392
pH after IUT	7.26 (7.01-7.31)	7.32 (7.28-7.36)	0.897
Platelets before IUT (10^9/mL)	79 (65-85)	86 (85-87)	0.088
Platelets after IUT (10^9/mL)	138 (130-146)	141 (115-154)	0.831
Transfused blood volume (mL)	25 (22.5-45.0)	26 (19.0-33.0)	0.721
Procedure-related complications	4 (21.4%)	1 (25.0%)	0.987
Resolution of infection after IUT	4 (28.6%)	2 (50.0%)	0.569
Fetal loss after IUT	2 (16.7%)	0 (0.0%)	0.550
Number of IUTs	2 (1-3)	1 (1-1)	0.090
Time interval between maternal infection diagnosis and IUT (in days)	21 (15-27)	33 (28-37)	0.050

Data are expressed as median (Q_1–Q_3) for continuous variables and number (percentage) for categorical variables. p-values were calculated using the Student's t-test or Mann–Whitney U test for continuous variables, and Pearson's chi-square test or Fisher's exact test for categorical variables IUT: Intrauterine Transfusion; MoM: Multiples of the Median; Hb: Hemoglobin; pH: Potential of Hydrogen. Sixteen hydropic fetuses met criteria for transfusion; however, two experienced intrauterine demise before the procedure.

Results

A total of 41 pregnant women diagnosed with parvovirus B19 infection were included in the study. Of these, 29 fetuses (70.7%) presented with hydrops fetalis, and 12 fetuses (29.3%) were non-hydropic at the time of diagnosis. Maternal age was significantly higher in the hydropic group compared to the non-hydropic group (median:30 vs. 28 years, p=0.021). Gravidity (p=0.004) and parity (p=0.030) were both lower in the hydropic group, and nulliparity was more common (58.6% vs. 16.7%, p=0.019). Ultrasonographic findings revealed that ascites (86.2% vs. 77.8%, p=0.049), pericardial effusion (86.2% vs. 8.3%, p=0.001), pulmonary effusion (65.5% vs. 25.0%, p=0.014), skin edema (75.9% vs. 0%, p=0.001), placentomegaly (55.1% vs. 16.6%, p=0.022), and cardiomegaly (37.9% vs. 0%, p=0.018) were significantly more frequent in the hydropic group. MCA peak systolic velocity was significantly higher in the hydropic group (median: 60.0 vs. 38.0 cm/s, p=0.002), as was the MoM value (1.67 vs. 1.35, p=0.049). Spontaneous resolution of infection was more common in non-hydropic fetuses (50.0% vs. 12.0%, p=0.036). Live birth was significantly less frequent in hydropic cases (48.2% vs. 83.3%, p=0.044), while perinatal death

was higher (37.9% vs. 16.7%, p=0.047). Four hydropic fetuses resulted in miscarriage before 20 weeks; none occurred in the non-hydropic group. (Table 1) Among the 16 hydropic fetuses who met criteria for intrauterine transfusion, two experienced fetal demise before the procedure, IUT was performed in 14 hydropic and 4 non-hydropic fetuses. Pre-transfusion hemoglobin levels were significantly lower in hydropic fetuses (4.7 vs. 8.2 g/dL, p=0.010), while other laboratory and procedural parameters—including post-transfusion hemoglobin, pH, platelet counts, transfused volume, and complication rates—were similar between groups. Although not statistically significant, the time interval between maternal diagnosis and IUT was shorter in hydropic cases (21 vs. 33 days, p=0.050). (Table 2) Among liveborn infants, hydropic fetuses had lower gestational age at delivery (median: 34 vs. 36 weeks, p=0.025) and lower Apgar scores at both 1st and 5th minutes (p=0.006 and p=0.008, respectively). Fetal distress was more frequent in the hydropic group (52.0% vs. 16.7%, p=0.043), and neonatal anemia and postnatal transfusion requirements were also significantly higher (both p=0.044). NICU stay was longer in hydropic neonates (median:16 vs. 7 days, p=0.003). Other variables such as respiratory support, cranial abnormalities, and neonatal PCR positivity did not differ significantly between groups. (Table 3).

Table 3: Comprehensive Comparison of Neonatal Outcomes Between Hydropic and Non-Hydropic Fetuses Affected by Parvovirus B19 Infection

	Hydropic fetuses n:25 (70.7%)	**Non-hydropic fetuses n:12 (29.3%)**	**p value**
Gestational age at delivery (week)	34 (31-36)	36 (34-37)	0.025
Mode of delivery			0.443
Vaginal birth	6 (24%)	5 (41.7%)	
Cesarean section	19 (76.0%)	7 (58.3%)	
Preterm Delivery	14 (56.0%)	4 (33.3%)	0.295
Birth weight (gram)	2500 (1860-3105)	2750 (2285-2970)	0.144
Fetal Distress	13 (52.0%)	2 (16.7%)	0.043
Apgar score at 1st minute	3 (2-6)	7 (4-8)	0.006
Apgar score at 5th minute	4 (2-7)	8 (4-9)	0.008
Umbilical cord pH	7.27 (6.99-7.32)	7.26 (7.19-7.34)	0.105
Fetal Hemoglobin Level	12.9 (10.9-17.0)	17.1 (16.0-18.8)	0.046
Fetal Hematocrit Level	41.2 (36.5-54.5)	58.3 (51.5-59.0)	0.119
Fetal Platelet Level	176 (124-255)	170 (149-200)	0.803
Neonatal anemia	7 (50.0%)	1(10.0%)	0.044
Need for postnatal transfusion	7 (50.0%)	1(10.0%)	0.044
Thrombocytopenia at birth	4 (28.5%)	0 (0.0%)	0.107
Neonatal Parvovirus B19 PCR positivity	3 (21.4%)	0 (0.0%)	0.245
Abnormal cranial findings	2 (14.2%)	0 (0.0%)	0.505
Total duration of NICU stay (days)	16 (14-30)	7 (5-12)	0.003
Transient tachypnea of the newborn	9 (%64.2)	5 (%50.0)	0.285
Respiratory distress syndrome	10 (71.4%)	7 (70.0%)	0.940
Continuous positive airway pressure	11 (78.5%)	8 (80.0%)	0.898
Mechanical ventilation	10 (71.4%)	7 (70.0%)	0.940
Phototherapy for neonates	1 (7.1%)	4 (40.0%)	0.122
Intracranial hemorrhage	1 (7.1%)	0 (0.0%)	1.000
NICU admission	13 (92.9%)	7 (70.0%)	0.138

Data are expressed as median (Q_1–Q_3) for continuous variables and number (percentage) for categorical variables. p-values were calculated using the Student's t-test or Mann–Whitney U test for continuous variables, and Pearson's chi-square test or Fisher's exact test for categorical variables NICU: Neonatal Intensive Care Unit; PCR: Polymerase Chain Reaction; IUT: Intrauterine Transfusion; RDS: Respiratory Distress Syndrome; CPAP: Continuous Positive Airway Pressure; Hb: Hemoglobin. Percentages were calculated based on liveborn infants in each group.

Dıscussion

Our findings suggest that fetal hydrops is a critical prognostic marker in parvovirus B19 infection, being strongly associated with adverse perinatal outcomes. In our series, hydropic fetuses had a live birth rate of 48% compared with 83% in non-hydropic cases, and a perinatal mortality of 38% versus 17%. These results align with the meta-analysis by Bascietto et al., which demonstrated markedly increased risks of miscarriage and perinatal death in hydropic fetuses (10). Almost all fetal losses in our cohort occurred in the hydropic group, particularly in cases diagnosed before 20 weeks, consistent with prospective studies showing that most losses after maternal parvovirus infection occur during the first half of pregnancy (5,11). Although our high incidence of hydrops (70.7%) reflects referral bias to a tertiary center, it underscores the poor prognosis once hydrops develops. Importantly, spontaneous resolution occurred in only 12% of hydropic cases versus 50% of non-hydropic fetuses, paralleling previous reports (3,10). Ultrasonographic findings reflected the pathophysiology of severe fetal anemia. Hydropic fetuses more frequently exhibited ascites, skin edema, pericardial and pleural effusions, cardiomegaly, and placentomegaly, consistent with the cascade of viral erythroid suppression, profound anemia, and high-output cardiac failure (3). Ascites was often the earliest sign, followed by serous effusions, while placentomegaly likely represented compensatory hypertrophy due to hypoxia or cardiac strain. Some non-hydropic fetuses with limited findings—such as isolated ascites—resolved spontaneously, supporting the concept of partial or incomplete disease manifestations, as described by Olejniczak et al. and Macé et al. (4,7). These observations emphasize the importance of close surveillance even in apparently mild cases(12). MCA Doppler played a pivotal role in monitoring and guiding intervention. In our study, PSV values were significantly higher in hydropic fetuses (median 1.67 MoM) than in non-hydropic ones (1.35 MoM), reflecting the severity of anemia. Cosmi et al. demonstrated that MCA-PSV >1.5 MoM has >90% sensitivity and specificity for detecting moderate-to-severe anemia(13). All transfused fetuses in our cohort exceeded this threshold, and our protocol of intervening once MCA-PSV rose above 1.5 MoM or when early hydrops appeared was consistent with international guidelines (3,14). This surveillance allows timely detection of fetal anemia before the development of hydrops fetalis. Early intervention is critical because hydrops (generalized fetal edema due to high-output cardiac failure from anemia) is associated with a much higher risk of fetal loss. Therefore, our protocol was to perform an IUT as soon as MCA-PSV rose above 1.5 MoM or if any signs of incipient hydrops appeared, rather than waiting for frank hydrops to develop. We adhered closely to current recommendations in this regard, ensuring our management was in line with international guidelines (5,6). Parvovirus B19 infection leads to severe fetal aplastic anemia**,** and this was reflected in the hematological parameters of our cases. Pre-transfusion fetal hemoglobin (Hb) levels were markedly low, confirming significant anemia at diagnosis. In hydropic fetuses, initial cord blood Hb measurements were often only a few g/dL (often less than 5 g/dL). For example, Vanage et al. reported mean fetal Hgb around 4 g/dL before IUT in parvovirus-related hydrops, which increased to ~11 g/dL after transfusion(15). In our series, we similarly observed a substantial rise in fetal hemoglobin immediately after IUT. We aimed to raise the fetal Hb into the high normal range for gestation with each transfusion, typically achieving increases on the order of 5–7 g/dL per procedure. This drastic improvement in oxygen-carrying capacity often led to rapid reversal of abnormal fetal hemodynamics. Correspondingly, the MCA-PSV, which was elevated pre-transfusion, fell to normal levels following transfusion as anemia was corrected (2). Fetal ultrasound signs of cardiac strain (such as tachycardia and cardiomegaly) also stabilized after hemoglobin restoration. The overall survival rates reported in our cohort 88.9% in transfused fetuses are consistent with large multicenter studies of IUT in parvovirus B19 infection, such as those by Kosian et al. (84.5%), Schild et al. (83.8%), and Berezowsky et al. (83%) (16–18) . Similar to these studies, we observed that survival was highly dependent on hydrops status. In our cohort, non-hydropic fetuses had a survival rate of 83.3%, while hydropic fetuses had significantly lower survival (48.2%), a pattern closely matching outcomes reported by Nagel et al., who found 66.7% survival in hydropic cases, and Hellmund et al., who observed ~50–60% survival in hydropic fetuses transfused before 20 weeks (19,20). These findings reaffirm that hydrops remains the strongest predictor of perinatal mortality, despite optimal intervention. In our cohort, the mean gestational age at first intrauterine transfusion was 26 weeks—later than the 19+3 weeks reported by Kosian et al. and the 16+6 weeks by Hellmund et al.(16,19). This delay likely reflects real-world factors such as delayed diagnosis, referral from

peripheral centers, or the subacute progression of fetal anemia. Importantly, our outcomes demonstrate that IUT remains technically feasible and clinically effective even when performed in the late second or early third trimester. While earlier transfusions are more frequently reported in the literature, gestational age alone has not been shown to independently influence survival when fetal condition and hydrops status are accounted for. Our findings support the principle that the decision to transfuse should be based on fetal MCA Doppler findings and clinical status, rather than fixed gestational age thresholds. This has particular relevance for healthcare settings where early serologic screening or Doppler surveillance may not be uniformly implemented. Overall, our experience adds to the growing evidence that timely diagnosis and prompt intervention—regardless of gestational age—are key determinants of favorable outcomes in parvovirus B19–related fetal anemia. Our observed hematologic response to IUT—an average hemoglobin increase of 5–7 g/dL and rapid normalization of MCA-PSV—is consistent with outcomes reported by Vanage et al. and Cosmi et al. (13,15). Pre-transfusion hemoglobin levels in our hydropic cases (mean 4.7 g/dL) were nearly identical to those reported by Nagel et al. and Kosian et al. (16,20). Post-transfusion resolution of acidosis and improvement in fetal Doppler profiles further confirm the physiologic efficacy of IUT in reversing parvovirus-induced anemia. Thrombocytopenia was frequent among hydropic fetuses in our series, consistent with de Jong et al., who reported significantly lower platelet counts in non-survivors (16,21). While no platelet transfusions were ultimately required in our cohort, we adopted a preparedness protocol for co-transfusion when platelets fell below critical thresholds. This cautious approach is supported by transfusion guidelines and studies reporting fetal platelet suppression during parvovirus viremia(22). Moreover, as with prior studies, our transfused fetuses—especially non-hydropic—rarely required more than one or two procedures. Kosian et al. reported a mean of 1.8 IUTs per fetus [16], and Hellmund et al. described a similar mean in early-transfusion cases (16). This limited transfusion burden underscores the transient nature of parvovirus-induced aplasia, in contrast to conditions like red cell alloimmunization that often require serial IUTs throughout gestation.

We documented no procedure-related fetal losses and a minor complication rate of 21.4% in hydropic fetuses and 25.0% in non-hydropic fetuses , which falls within the range reported by other high-volume centers (10–30%) (15,16). Complications such as transient fetal bradycardia or minor cord hematomas were self-limited. This confirms that with experienced operators and modern ultrasound guidance, IUT for parvovirus B19 anemia is technically feasible and safe, including when performed before 20 weeks' gestation (19). Neonatal outcomes mirrored the in-utero severity of illness. Hydropic infants were delivered at a significantly earlier gestational age (median 34 weeks) and had lower Apgar scores and higher rates of fetal distress. These neonates also required longer NICU stays (median 16 days vs 7 days), and nearly half had neonatal anemia requiring postnatal transfusion. In contrast, most non-hydropic infants were delivered at later gestational ages with minimal complications. Our findings align with those of Attwood et al., who reported that hydropic neonates often experience more intensive care needs and greater perinatal morbidity compared to their non-hydropic counterparts (9). Interestingly, we observed no significant difference in abnormal cranial imaging or neurological complications at discharge between groups. Although our follow-up was limited to the neonatal period, this is in line with the work of Miller et al., who found no increase in congenital anomalies or neurodevelopmental impairment in parvovirus-exposed children without hydrops (11). Nonetheless, longer-term studies suggest that survivors of fetal hydrops may carry a small but increased risk of neurodevelopmental delay, likely related to periods of intrauterine hypoxia (20). For instance, de Jong et al. reported that 11% of infants treated with IUT for parvovirus-related anemia exhibited significant neurodevelopmental impairments by early childhood (21). Our findings reinforce the growing consensus that while fetal hydrops substantially worsens prognosis, survival can be markedly improved through early diagnosis and timely intrauterine transfusion. This underscores the critical importance of MCA Doppler surveillance and centralized fetal therapy expertise in the management of parvovirus B19 infection. However, the study is not without limitations. The small overall sample size and the numerical imbalance between hydropic and non-hydropic groups—particularly within the IUT subgroup—limit the statistical power of intergroup comparisons. Therefore, these findings should be interpreted with caution. The high proportion of hydropic fetuses likely reflects referral bias inherent to a tertiary care setting, where severe and complicated cases are preferentially referred. Consequently, our findings may not fully represent

the general population distribution of parvovirus B19 infection. Its retrospective nature introduces potential for selection bias, and the relatively small sample size limits statistical power. Another major limitation of this study is the absence of long-term neurodevelopmental follow-up data, particularly for hydropic survivors who underwent IUT. Future multicenter studies with extended follow-up are needed to evaluate potential neurodevelopmental sequelae related to intrauterine hypoxia.

Study Limitations: This study has several limitations that should be acknowledged. First, its retrospective design inherently carries the risk of selection bias and limits control over confounding variables. Second, the relatively small sample size—particularly within the non-hydropic and intrauterine transfusion subgroups—may have reduced the statistical power for some intergroup comparisons. Third, as a tertiary referral center, our cohort included a disproportionately high number of severe cases, which likely contributed to the high incidence of fetal hydrops and may limit the generalizability of our findings to the broader population. In addition, the timing of diagnosis and referral varied among patients, potentially influencing disease severity and outcomes at presentation. Finally, long-term neurodevelopmental follow-up data were not available, particularly for hydropic survivors who underwent intrauterine transfusion, preventing assessment of potential late sequelae related to intrauterine hypoxia. Future multicenter, prospective studies with larger sample sizes and long-term follow-up are needed to better define prognosis and optimize management strategies in fetal parvovirus B19 infection.ekek

Conclusion

Our study demonstrates that fetal hydrops remains the most significant predictor of adverse perinatal outcomes in parvovirus B19 infection, whereas non-hydropic fetuses generally have an excellent prognosis. Intrauterine transfusion, guided by MCA Doppler surveillance, is a safe and effective treatment for parvovirus B19–related fetal anemia, even when performed in the late second trimester. These findings highlight the critical importance of early diagnosis, timely referral to specialized fetal medicine centers, and prompt intervention to improve survival and reduce perinatal morbidity, particularly in hydropic cases

Ethics approval and consent to participate: Approval was obtained from the Institutional Review Board of Ankara Etlik City Hospital (approval number: AESH-BADEK2–2025-027).

Competing interests: The authors declare no conflicts of interest.

Funding: The study did not receive funding.

Author contributions:

Concept: RD, DDB, MAO, BTC

Design RD, DDB, MAO, BTC

Data Collection or Processing: RD, DDB, MAO, BTC

Analysis or Interpretation: RD, DDB, MAO, BTC

Literature Review: RD, DDB, MAO, BTC, SC

Writing: RD, DDB, MAO, BTC, SC

Critical Review: RD, DDB, MAO, BTC, SC

Availability of data and materials: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. Malutan AM, Ormindean CM, Diculescu D, Ciortea R, Nicula R, Pop D, et al. Parvovirus B19 in Pregnancy—Do We Screen for Fifth Disease or Not? Life. 2024 Dec;14(12):1667.
2. Jensen IP, Thorsen P, Jeune B, Møller BR, Vestergaard BF. An epidemic of parvovirus B19 in a population of 3,596 pregnant women: a study of sociodemographic and medical risk factors. BJOG Int J Obstet Gynaecol. 2000 May;107(5):637–43.
3. Kagan KO, Hoopmann M, Geipel A, Sonek J, Enders M. Prenatal parvovirus B19 infection. Arch Gynecol Obstet. 2024 July 29;310(5):2363–71.
4. Olejniczak O, Kornacki J, Boroń D, Gutaj P, Iciek R, Wender-Ożegowska E. Parvovirus B19 Infection in Pregnancy—Course of the Disease, Fetal Complications and Management Tools: A Case Series and Literature Review. Children. 2024 Sept;11(9):1037.
5. Enders M, Weidner A, Zoellner I, Searle K, Enders G. Fetal morbidity and mortality after acute human parvovirus B19 infection in pregnancy: prospective evaluation of 1018 cases. Prenat Diagn. 2004 July;24(7):513–8.
6. Bertoldi A, Colazo Salbetti MB, Rodríguez G, Tenaglia M, Hernández G, Alfaro J, et al. Human parvovirus B19 infection in a pregnant patient resulting in severe hydrops, foetal death and persistent infection. Access Microbiol. 2022;4(10) :000428.

7. Macé G, Sauvan M, Castaigne V, Moutard ML, Cortey A, Maisonneuve E, et al. Clinical presentation and outcome of 20 fetuses with parvovirus B19 infection complicated by severe anemia and/or fetal hydrops. Prenat Diagn. 2014 Nov;34(11):1023–30.
8. Torcia E, Familiari A, Passananti E, Alesi MV, di Marco G, Romanzi F, et al. Parvovirus B19 Infection in Pregnancy: Awareness of the Increased Incidence of Severe Intrauterine Infection. Diagnostics. 2025 May 31;15(11):1397.
9. Attwood LO, Holmes NE, Hui L. Identification and management of congenital parvovirus B19 infection. Prenat Diagn. 2020 Dec;40(13):1722–31.
10. Bascietto F, Liberati M, Murgano D, Buca D, Iacovelli A, Flacco ME, et al. Outcome of fetuses with congenital parvovirus B19 infection: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2018 Nov;52(5):569–76.
11. Miller E, Fairley CK, Cohen BJ, Seng C. Immediate and long term outcome of human parvovirus B19 infection in pregnancy. Br J Obstet Gynaecol. 1998 Feb;105(2):174–8.
12. Lamont RF, Sobel J, Vaisbuch E, Kusanovic JP, Mazaki-Tovi S, Kim SK, et al. Parvovirus B19 Infection in Human Pregnancy. BJOG Int J Obstet Gynaecol. 2011 Jan;118(2):175–86.
13. Cosmi E, Mari G, Delle Chiaie L, Detti L, Akiyama M, Murphy J, et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia resulting from parvovirus infection. Am J Obstet Gynecol. 2002 Nov;187(5):1290–3.
14. Crane J, Mundle W, Boucoiran I, Maternal Fetal Medıcıne Commıttee. Parvovirus B19 infection in pregnancy. J Obstet Gynaecol Can JOGC J Obstet Gynecol Can JOGC. 2014 Dec;36(12):1107–16.
15. Vanage U, Kitova J, Machtejeviene E. Impact of Intrauterine Blood Transfusion in Managing Severe Fetal Anemia Induced by Parvovirus B19 FMF Congress]; 2024
16. Kosian P, Hellmund A, Geipel A, Bald R, Geist OM, Böckenhoff P, et al. Intrauterine transfusion in 103 fetuses with severe anemia caused by parvovirus infection. A multicenter retrospective study. Arch Gynecol Obstet. 2022 Aug 2;308(1):117–25.
17. Berezowsky A, Hochberg A, Regev N, Weisz B, Lipitz S, Yinon Y. Intrauterine Blood Transfusion for Parvo B19-Induced Fetal Anemia: Neuroimaging Findings and Long-Term Neurological Outcomes. Fetal Diagn Ther. 2023 Sept;50(3):206–14.
18. Intrauterine management of fetal parvovirus B19 infection - Schild - 1999 - Ultrasound in Obstetrics & Gynecology - Wiley Online Library 1999 Mar;13(3):161–166.
19. Hellmund A, Geipel A, Berg C, Bald R, Gembruch U. Early Intrauterine Transfusion in Fetuses with Severe Anemia Caused by Parvovirus B19 Infection. Fetal Diagn Ther. 2018;43(2):129–37.
20. Nagel HTC, De Haan TR, Vandenbussche FPHA, Oepkes D, Walther FJ. Long-Term Outcome After Fetal Transfusion for Hydrops Associated With Parvovirus B19 Infection: Obstet Gynecol. 2007 Jan;109(1):42–7.
21. De Jong EP, Lindenburg IT, van Klink JM, Oepkes D, van Kamp IL, Walther FJ, et al. Intrauterine transfusion for parvovirus B19 infection: long-term neurodevelopmental outcome. Am J Obstet Gynecol. 2012 Mar;206(3):204.e1-5.
22. Segata M, Chaoui R, Khalek N, Bahado-Singh R, Paidas MJ, Mari G. Fetal thrombocytopenia secondary to parvovirus infection. Am J Obstet Gynecol. 2007 Jan 1;196(1):61.e1-61.e4.