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Case Report

Transfusion Medicine Section

Managing Severe Foetal Anaemia Due to Rh Alloimmunisation: A Report of Two Cases of Successful Intrauterine Blood Transfusion

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ABSTRACT

Intrauterine Transfusion (IUT) remains a critical intervention in managing severe foetal anaemia, particularly due to Red Blood Cell (RBC) alloimmunisation. Without timely treatment, foetal anaemia can lead to hydrops foetalis, heart failure, or even intrauterine death. The decision to perform IUT is guided by key clinical indicators such as raised Middle Cerebral Artery Peak Systolic Velocity (MCA-PSV), decreased foetal haemoglobin, and high maternal antibody titres. Although IUT has significantly improved foetal and neonatal outcomes, it requires precise timing, well-coordinated teamwork, and careful preparation of compatible donor blood to minimise complications. In the present report, both cases involved Rh-negative women with known alloimmunisation who presented in the third trimester with rising antibody levels and ultrasound findings suggestive of foetal anaemia. The transfusions were performed under ultrasound guidance via umbilical vein puncture. Blood prepared for Intrauterine Transfusion (IUT) was group O RhD-negative, leukocyte-depleted, irradiated, and crossmatch-compatible with the maternal sample. Foetal haemoglobin and haematocrit levels were assessed before, during, and after the transfusion, with close monitoring maintained until delivery and throughout the neonatal period. In the first case, two well-timed transfusions improved foetal haemoglobin and normalised MCA-PSV, resulting in the birth of a stable neonate who later required exchange transfusion and phototherapy but recovered fully. The second mother received one IUT but declined further treatment despite worsening MCA-PSV. Due to foetal distress, an emergency caesarean section was performed. The preterm infant responded well to a double-volume exchange transfusion and phototherapy. Both babies remained stable during follow-up, with one requiring a top-up transfusion for delayed haemolysis.

Keywords: Blood group incompatibility, Cordocentesis, Foetal blood transfusion, Haemolytic disease of the newborn, Hydrops foetalis, Intrauterine transfusion, Prenatal, Ultrasonography

Case 1

A pregnant woman in her 20's, gravida 3, para 1, living 1, abortion 1 (G3P1L1A1), at 29 weeks and 3 days of gestation, was admitted for further evaluation of Rh isoimmunisation. She had a prior Lower Segment Caesarean Section (LSCS) performed three years earlier for meconium-stained amniotic fluid, resulting in the birth of a healthy female infant weighing 3 kg. Her obstetric history also included a missed abortion in 2020, which was managed medically. The current pregnancy was spontaneous and confirmed by a urine pregnancy test at approximately 45 days of amenorrhoea.

Routine antenatal screening revealed that the mother was blood group AB Rh-negative, with a positive Indirect Coombs Test (ICT). Her husband's blood type was A positive. The pregnancy progressed without complications—she had no symptoms of abdominal pain, vaginal bleeding, or discharge and reported regular foetal movements. First-trimester assessments, including the dating and nuchal translucency scans, were normal. The second-trimester anomaly scan was also reassuring. She received both doses of tetanus toxoid as scheduled and had no history of chronic illness, gestational diabetes, or hypertension. The patient adhered to routine antenatal supplementation with iron, folic acid, and calcium.

At 34 weeks of gestation, antibody identification confirmed the presence of anti-D, and the subsequent indirect antibody titre was 1:64. Following this, foetal Doppler assessment revealed a raised Middle Cerebral Artery Peak Systolic Velocity (MCA-PSV) of 1.79 MoM, suggestive of foetal anaemia. Given the rising antibody titres along with Doppler evidence of anaemia, a decision was made to proceed with an Intrauterine Transfusion (IUT).

Prior to the IUT procedure, corticosteroids were administered to promote foetal lung maturity. A unit of O Rh-negative Packed Red Blood Cells (PRBCs), collected within 72 hours, was specially prepared—leukocyte filtered, irradiated, and double-packed to achieve a haematocrit more than 80% and crossmatched with maternal serum.

Cordocentesis was performed as part of the pre-transfusion evaluation to determine foetal blood group, Rh status, hemoglobin level, haematocrit, and Direct Coombs Test (DCT). The foetus was determined to have a B RhD-positive blood group, with a haemoglobin level of 6.5 g/dL, a reticulocyte count of 16.7%, and a DCT positive result. At 31 weeks + 1 day of gestation, the first IUT was successfully performed. A total of 80 mL of PRBCs was transfused, resulting in an increase in foetal haemoglobin to 13 g/dL and haematocrit to 35%, as shown in [Table/Fig-1].

IUT-1	Hb	HCT	IUT-2	Hb	HCT
Initial before IUT	6.7	20.7	Initial Before IUT	7.9	23.7
After 30 mL	9.1	27.1	After 30 mL	11.0	33
After 60 mL	11	33	After 60 mL	10.6	31.8
After 70 mL repeat	13.7	41	After 60 mL repeat	10.9	32.7
After 80 mL transfused	14.3	42.9	After 80 mL transfused	11.7	35.1

[Table/Fig-1]: Types of implants used and haemoglobin values in IUT 1 and IUT 2.

Haemoglobin Values Checked using Haemocue

Ultrasonography (USG) at 31 weeks + 2 days revealed foetal isoimmunisation with foetal anaemia, without evidence of cardiac failure, following IUT. The MCA-PSV was 1.32 MoM. In view of foetal

anaemia, with haemoglobin of 7.9 g/dL and haematocrit of 23.7% 33 weeks +3 days of gestation, the second IUT was carried out, which further improved haemoglobin to 11.7 g/dL and haematocrit to 35.1%, with MCA-PSV decreasing to 1.5 MoM as shown in [Table/Fig-2].

	Pre IUT	Post IUT-1	Post IUT-2
Hb	6.5	13	11.7
PCV	20%	35%	35.1%
MCA-PSV	1.79 MoM	1.32 MoM	1.5 MoM

[Table/Fig-2]: Pre IUT transfusion and post IUT transfusion values.

At 33 weeks + 6 days, the patient presented in preterm labour and underwent an emergency caesarean section. A male neonate birth weight of 2 kg was delivered.

Case 2

A pregnant woman in her 20's gravida 3, para 1, live 1, with one prior intrauterine death (G3P1L1D1), conceived spontaneously and confirmed pregnancy with a urine test at 6 weeks of gestation. Her last menstrual period was April 28, 2024, and her estimated due date was February 2, 2025. She had a history of a LSCS performed in 2016 during her first pregnancy due to obstetric reasons. The newborn from that pregnancy was Rh-positive, and she had received postpartum anti-D prophylaxis. Her second pregnancy, complicated by a foetal anomaly, resulted in foetal demise and required a hysterotomy at 34 weeks.

In the current pregnancy, the first trimester progressed without complications. She was on regular folic acid, underwent a normal dating ultrasound, and first-trimester screening indicated low risk.There were no signs of infection, fever, medication abuse, or teratogen exposure. By the fifth month, she started perceiving foetal movements. She continued iron and calcium supplementation and received both doses of tetanus toxoid.

During the second trimester, an Oral Glucose Tolerance Test (OGTT) revealed elevated values, leading to the diagnosis of Gestational Diabetes Mellitus (GDM), for which she was started on Metformin 250 mg twice daily. She was also being treated for hypothyroidism with thyroxine 75 mcg daily. Her blood type was B Rh-negative, while her husband was O Rh-positive.

At around 17 weeks of gestation, ICT was positive; with further testing anti-D antibody was identified. The Incomplete Antibody Titre (IAT), initially low, began to rise to 1:16 by 17 weeks and increased to 1:64 by 24 weeks. The elevated levels persisted through 31 weeks of gestation as shown in [Table/Fig-3]. (Due to the rising titres, she was referred to a foetal medicine specialist for closer monitoring). Serial anomaly and growth ultrasounds remained within normal limits. Although the MCA-PSV was initially under 1.5 Multiples of the Median (MoM), it began to increase as she entered the third trimester.

Gestation age in weeks	IAT	Growth scan
17	1:16 positive	Showed growth satisfactory
21	1:32 positive	Showed growth satisfactory
24	1:64 positive	Not available
29	1:64 positive	Not available
31	1:64 positive	MCA-PSV 71.8 CM second on 1.68 MOM

[Table/Fig-3]: IAT TITRE.

She presented at 31 weeks and 6 days of gestation for ongoing evaluation of Rh isoimmunisation. Doppler ultrasound showed an MCA-PSV of1.68 MoM, suggestive of moderate foetal anaemia. Based on this, an IUT was planned and scheduled at 31 weeks of gestation.

Prior to the procedure, blood products were prepared. This included double-packed red blood cells of O Rh-negative type, with a haematocrit of 80%. These units were collected within 72 hours, leukoreduced, irradiated, and cross-match compatible with maternal serum.

Cord blood analysis before the IUT blood group showed O Rh D positive, haemoglobin level of 4 g/dL and DCT positive using the column agglutination technology. Total bilirubin was found to be elevated at 6.96 mg/dL, with a predominantly indirect component. During the IUT, the fetus received 80 mL of red blood cells, which led to a significant rise in haemoglobin—from 4 g/dL to 14.3 g/dL post-transfusion as shown in [Table/Fig-4].

Transfusion stage/ parameters	Before IUT (Initial)	After 30 mL transfusion	After 60 mL transfusion	After 80 mL transfusion
Hemoglobin (g/dL)	4.0	10.5	11.0	14.3
Haematocrit (%)	18%	31.5	33	42.9

[Table/Fig-4]: Pre IUT and post IUT value.

Following the transfusion, serial Doppler monitoring of the MCA-PSV was conducted. Initially, the values stabilised, but over time, they began to rise again, ranging between 1.36 and 1.6 MoM. Despite thorough counselling about the benefits of repeat intervention, the patient declined a second IUT.

Due to the progressive increase in MCA-PSV and concerns about potential foetal compromise, an emergency LSCS was planned. Blood was arranged in preparation for delivery. Antibody screening at this stage confirmed the presence of anti-D antibodies. B Rh-negative unit and O Rh-negative unit were compatible.

A moderate preterm male baby was delivered via breech extraction during the emergency caesarean. He weighed 1.98 kg. At birth, he was apnoeic but responded positively to tactile stimulation. He was started on Continuous Positive Airway Pressure (CPAP) at minimal settings with 21% FiO_2. The umbilical cord was clamped promptly, and the newborn was transferred to the neonatal care unit.

RESULTS

These two cases highlight how timely IUTs can make a significant difference when dealing with Rh alloimmunisation and foetal anaemia, helping to stabilise the fetus and improve neonatal outcomes. In the first case, the patient came in during the third trimester with rising anti-D antibodies and increased MCA-PSV, indicating developing foetal anaemia. Two IUTs were carried out, both leading to a marked improvement in the baby's haemoglobin levels, which had initially been critically low. A few weeks later, the patient went into preterm labour and underwent an emergency caesarean section, delivering a male baby. The newborn, B Rh-positive with a positive DCT, initially needed respiratory support and was treated with phototherapy and an exchange transfusion. The baby responded well and was discharged in stable condition after two weeks in the Neonatal Intensive Care Unit (NICU).

In the second case, the patient—also in the third trimester—was referred due to foetal anaemia on Doppler assessment, in the setting of known Rh isoimmunisation and other health issues including gestational diabetes and hypothyroidism. An IUT was performed after tests showed the fetus had significant anaemia, with low haemoglobin and haematocrit levels.Post-transfusion measurements confirmed a good rise in both parameters. Although follow-up scans showed continued elevated MCA-PSV and a second transfusion was recommended, the patient chose not to proceed with further in-utero treatment.Due to the foetal condition (anaemia and increasing MCA-PSV), an emergency C-section

was performed. The baby was delivered in breech position and had mild respiratory issues at birth, which were quickly managed with non-invasive support. Blood tests showed anaemia and elevated bilirubin, which were treated successfully with exchange transfusion, phototherapy, and a top-up of red blood cells. The newborn responded well to treatment and was later discharged in stable condition.

DISCUSSION

Intrauterine transfusion was introduced in 1963 by Liley who used an intraperitoneal approach [1]. Almost 20 years later the procedure was improved to a transfusion into the umbilical vein under constant ultrasonographic guidance. During pregnancy, women with known RBC alloimmunisation and/or a history of Haemolytic Disease of the Foetus and Newborn (HDFN) are closely monitored using antibody titres [1]. The fetus is also closely monitored throughout the pregnancy to check for foetal wellbeing and foetal anaemia and to determine the best time to deliver. The severe anaemia may cause cardiovascular failure, tissue hypoxia, and death in utero. IUT may be lifesaving in these circumstances (a procedure in which red blood cells from a donor are injected into the fetus when the fetus has anaemia). Untreated foetal anaemia can cause hydrops foetalis (foetal heart failure), severe life threatening swelling (edema) in an unborn baby.

Intrauterine transfusion is a vital procedure used to manage foetal anaemia, especially in pregnancies where the mother has developed antibodies against the baby's red blood cells (a condition known as RBC alloimmunisation). It is usually done when there are clear signs that the fetus is in trouble—like increased blood flow in the brain (measured by MCA-PSV), visible swelling from hydrops foetalis seen on ultrasound, low haemoglobin levels detected through cordocentesis, or rising bilirubin levels in the amniotic fluid. During the procedure, donor red blood cells are injected directly into the baby's umbilical vein to increase haemoglobin levels and prevent complications. This treatment often needs to be repeated every two to four weeks until the baby is ready to be delivered.

Although IUT can be life-saving, it is not without risks. Potential complications include infection, early labour, or triggering an immune response in the mother due to foetal blood mixing with hers. Even with its challenges, IUT has proven to be an effective treatment. Most foetus who received IUT transfusions especially those not severely affected by hydrops have good outcomes, with only a small percentage experiencing serious long-term issues like developmental delays or hearing and vision problems [1].

Preparing the Blood Unit for Intrauterine Transfusion (IUT)

Below are the essential requirements for preparing the blood unit for IUT: Crossmatching must be done using the mother's blood. If the mother is sensitised to the Rh D antigen, then O Rh D-negative packed red blood cells should be used. If sensitisation is to a different antigen, the blood should be type-specific. Screening for infections including HIV, Hepatitis B surface antigen, Hepatitis C virus, malaria, syphilis. The donor blood must be less than 72 hours old for IUT. Leukofiltered blood helps minimise the risk of Cytomegalovirus (CMV) transmission. Gamma irradiation (25 Gy) is necessary to prevent graft-versus-host disease, which can be life-threatening. A haematocrit level of 75-80% is required in the packed red blood cells.

Procedure

Begin by positioning the patient properly, and confirm the MCA-PSV to assess the need for IUT. Identify an accessible transfusion site—such as the umbilical vein within the foetal abdomen, the cord insertion point, or a free-floating loop of the umbilical cord.

Prepare the patient by administering local anaesthesia to the mother. Using a spinal needle, carefully access the foetal thigh through the maternal abdomen. An intramuscular injection of pancuronium (0.1 mg/kg based on the estimated foetal weight) is given to temporarily paralyse the fetus. Allow a few minutes for the medication to take effect. Pancuronium works by blocking neuromuscular activity, which helps reduce foetal movement and stabilise the foetal heart rate variability during the transfusion.

Set up the donor blood unit on an IV stand to ensure gravity-assisted flow. Connect the blood using a blood administration set and a three-way adapter fitted securely with a Luer lock and a 10 mL syringe, ensuring there are no air bubbles in the system. Collect a foetal blood sample in an EDTA tube to send for haemoglobin and haematocrit testing.

Calculate the required transfusion volume based on foetal needs and proceed with the transfusion carefully. At the end of IUT, flush the needle twice with normal saline take a sample for haemoglobin and haematocrit values. With draw the needle check for foetal cardiac activity, MCA-PSV.

The formula to calculate the volume of blood transfused is as follows:

$$\text{Volume to be transfused (mL)} = \frac{\text{Haematocrit of the donor RBC unit}}{\text{Foetal and placental blood volume (mL)}} \times \text{Desired increase in haematocrit}$$

Where:

Foetal and placental blood volume (mL) = Ultrasound estimated foetal weight (grams)×0.14 mL/gm.

The goal is to raise the foetal haematocrit to 0.45, and usually, an RBC unit with a haematocrit of 80% is used.

For fetuses requiring an IUT, the timing of delivery depends on the rate of fall in foetal Hb, gestation age, degree of foetal anaemia and time from last IUT [2].

IUT is a well-established treatment for foetal anaemia due to Rh isoimmunisation, but the complexity of the procedure can vary significantly depending on the pregnancy type and clinical condiction. The case series by Bansal V et al., sheds light on the added challenges that arise in multifoetal pregnancies, especially with twins and triplets, where anatomical, technical, and logistical difficulties can significantly complicate management. In contrast, our two recent singleton cases show how, even in less anatomically complex scenarios, careful timing and clinical decision-making are just as critical in achieving good outcomes.The first involved a twin pregnancy with a posterior placenta, which made it difficult to access the target fetus for transfusion. In another case, the mother had multiple atypical antibodies in addition to anti-D, which made cross-matching blood for transfusion extremely complicated. This highlights how maternal antibody profiles can directly impact the feasibility of IUT. Another twin case involved a monochorionic-diamniotic pregnancy, where vascular connections between the fetuses meant that transfusing one could unpredictably affect the other. The final and most complex case was a triplet pregnancy, where determining which cord belonged to which fetus, managing limited intrauterine space, and reducing the risk of early labour all added to the challenge [3].

While our cases involved singleton pregnancies, they were not without complications. Both patients presented in the third trimester with signs of foetal anaemia confirmed by elevated MCA-PSV on Doppler. In the first case, the fetus responded well to two IUTs, and although the baby was born prematurely and needed initial respiratory support, he recovered well with NICU

care. A late readmission for anaemia due to ongoing hemolysis further emphasised the need for long-term monitoring, even after successful transfusion and delivery. Notably, following birth, maternal-derived anti-D antibodies can remain in the infant's circulation for several months. These antibodies specifically target and bind to the D antigen present on Rh-positive red blood cells, leading to their immune-mediated destruction. As a result, when Rh-positive blood is used for transfusion, the anti-D antibodies react against the donor cells, causing cross-match incompatibility. This immunological response necessitates the use of Rh-negative, crossmatch compatible red blood cells for safe postnatal transfusion.

The second case involved a mother with comorbid conditions—gestational diabetes and hypothyroidism in addition to Rh alloimmunisation. After the first successful IUT, continued signs of anaemia were noted on follow-up. However, the patient declined further transfusions, which led to a decline in foetal condition and the need for an emergency caesarean. Fortunately, postnatal management, including phototherapy and exchange transfusion, helped stabilise the baby, who was later discharged in good condition.

Mari G et al.,'s crucial findings in 1995 demonstrated that measuring the peak systolic velocity in the foetal MCA is a highly effective way to detect foetal anaemia without invasive procedures. They found that when this velocity exceeds 1.5 MoM, it reliably indicates anaemia, showing near-perfect sensitivity and a relatively low false-positive rate of approximately 12% [4].

When comparing these cases, a few key differences are present. In Bansal V et al.,'s report, the challenges were largely technical—related to multiple fetuses, placental positioning, and limited intrauterine space. Our cases, however, emphasised the importance of decision-making, patient compliance, and managing maternal-foetal health as a whole. Even though singleton pregnancies are generally easier to handle procedurally, risks such as delayed hemolysis, maternal comorbidities, and refusal of further IUTs can have a significant impact on outcomes [5]. While Bansal V et al., successfully managed Rh isoimmunised triplets with a single round of IUT, preventing postnatal exchange transfusions, our singleton cases required more intensive postnatal care. One infant needed repeat transfusion weeks after birth due to delayed anaemia, and the other avoided further IUT but was delivered early for worsening foetal status. Both studies underscore that timely IUT improves outcomes, though clinical decisions and follow-up needs vary. Singleton or multifoetal, individualised care remains key [4]. In our Rh alloimmunisation cases, IUTs effectively corrected foetal anaemia and resulted in favourable neonatal outcomes, though some postnatal support was still necessary. In the case reported by Kapnosa Hasani RD et al., anti-M alloimmunisation was associated with an earlier onset of hydrops and the requirement for multiple transfusions, including postnatal transfusion support [6]. This underscores how the specific antibody involved and the timing of diagnosis can significantly influence disease severity and clinical course. Regardless of the underlying aetiology, vigilant surveillance and timely foetal intervention remain critical determinants of favourable outcomes. In contrast, both of our cases of Rh alloimmunisation demonstrated that well-timed IUTs can effectively correct foetal anaemia and result in favourable neonatal outcomes, even when limited postnatal management is required. Compared to the large series by Zwiers C et al., where complication rates were influenced by centre experience and technique, our smaller-scale results also support the value of catching foetal anaemia early—before hydrops sets in. Their findings showed a steady improvement in outcomes as methods evolved over time. Overall, these cases highlight how expert, timely intervention can make a major difference for both fetus and newborn [7]. Our experience aligns with the findings of Golia S et al., who also reported successful outcomes in Rh-alloimmunised pregnancies requiring IUT. However, while their study included 539 pregnant women, only 1.85% had unexpected red cell antibodies—primarily anti-D—and just two required IUT. In contrast, both of our cases involved severe foetal anaemia, highlighting a higher-risk subgroup. Anti-D was the most frequently identified antibody in both reports. Similarly, Golia S et al., observed that appropriate antenatal transfusion along with meticulous postnatal management—including exchange transfusion and phototherapy—played a crucial role in stabilising affected neonates and improving overall outcomes. Moreover, their data revealed that many Rh-negative women had not received anti-D prophylaxis, a factor that may explain the sensitisation. These observations emphasize the need for vigilant screening, timely intervention, and strict adherence to RhIg protocols to reduce the risk of HDFN [8]. Planning the next IUT can be guided by changes in MCA-PSV, using a lower threshold of 1.32 MoM rather than 1.5. As term approaches, careful timing of delivery becomes key, and after birth, babies often need close monitoring for jaundice and anaemia due to ongoing red cell breakdown [9]. IUT carries a small risk of foetal loss, which rises in cases with hydrops, early gestation, or technical complications. Using foetal paralytics, careful donor matching, and avoiding risky access points can reduce these risks. Long-term outcomes are generally good, with most babies developing normally, and delivery is ideally planned around term with prenatal prep like phenobarbital to lower postnatal complications [10]. Overall, these cases reinforce that while IUT is a lifesaving intervention, its success depends not just on technical skill but also on early diagnosis, individualised planning, and clear communication with the patient.

CONCLUSION(S)

Intrauterine transfusion is a reliable option for treating severe foetal anaemia, especially in pregnancies affected by alloimmunisation. With early diagnosis, close foetal monitoring, and timely transfusions, good neonatal outcomes are achievable. MCA-PSV trends can guide the timing of repeat procedures, often using a lower cutoff of about 1.32 MoM. As delivery approaches, balancing the final transfusion with the timing of birth is essential, and newborns require monitoring for jaundice and late anaemia. Although IUT carries a small risk—particularly in cases with hydrops or early gestation—careful technique, appropriate blood selection, and foetal paralysis help reduce complications. Most infants have favourable long-term outcomes, and planned near-term delivery further supports postnatal stability.

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