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Original article

How to manage fetomaternal hemorrhage? Description of five cases and literature review

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Abstract

Fetomaternal hemorrhage (FMH) is a poorly understood condition in which there is a transfer of fetal blood to the maternal circulation. It occurs in approximately 1-3 per 1,000 births. We described five cases with characteristics suggestive of both acute and chronic anemia. When FMH is suspected, maternal blood can be checked for the presence of fetal red blood cells and usually there are three diagnostic modalities: Kleihauer-Betke test, flow cytometry and Rosette test. The clinical manifestations and the prognosis of FMH depend on the gestational age, the volume of the hemorrhage and the rapidity with which it has occurred. Red blood transfusion is recommended, while in case with severe anemia and cardiac failure an exchange transfusion can be considered. The physician's awareness of the condition, the ability to suspect and diagnose it with appropriate testing have a significant impact on the epidemiology, accurate management and prognosis for the anemic neonates.

Keywords

Neonatal anemia, fetomaternal hemorrhage, blood transfusion, flow cytometry, exchange transfusion, newborn.

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Introduction

Fetomaternal hemorrhage (FMH) occurs when fetal blood crosses into the maternal circulation before or during delivery because the normal flow of blood within the placenta is disrupted. During normal pregnancies the transfer of small volumes of fetal blood into the maternal blood stream can be considered common for the leakage through the placental filter [1-3].

The incidence of moderate or severe FMH has been estimated to be approximately 1-3 per 1,000 births [4-7] and causing an estimated 14% of fetal deaths [8]. Although a number of etiologies have been associated with FMH, most causes remain unidentified [9]. The distinction between acute FMH and chronic FMH may be problematic but it's very important for the perinatal management. We have described five cases of FMH during the period from January 2014 and July 2016 that demonstrated characteristics suggestive of both acute and chronic anemia.

Case reports

Case report 1

A 30-year-old woman, gravida 0 para 0, presented to the delivery room in a first level hospital at $39^{4/7}$ weeks of gestation. Her prenatal laboratories and scans were unremarkable. Current pregnancy was uneventful. Spontaneous rupture of membranes occurred < 18 hours.

The infant, weighing 3.225 kg, adequate for gestational age (AGA), was delivered by an emergent cesarean section for recurrent fetal decelerations and she was born through meconium stained amniotic fluid.

At birth the newborn was noted to be markedly pale, hypotonic with mild cardiorespiratory depression responding to positive pressure ventilation (PPV) with mask. The Apgar scores were 7 and 8 at 1 and 5 minutes, respectively.

The mother's and infant's blood types were 0 positive and A positive respectively.

At one hour of life the baby showed progressive respiratory distress and need of oxygen (SpO_2 86-88% with FiO_2 0.3). She was still pale and a complete blood count showed a hemoglobin level (Hb) of 2.8 g/dl with a hematocrit (Ht) of 9.7% and red blood cell (RBC) count $0.8 \times 10^6/mm^3$. Metabolic acidosis (pH 7.21; acid base excess (ABE) -18.6 mmol/L; HCO_3 9.8 mmol/L; pCO_2 20.3 mmHg) treated with sodium bicarbonate and hypoglycemia corrected by bolus and infusion of glucose 10% were noted.

An immediate transfusion of 0-negative packed RBCs was started to treat anemia (20 ml/kg). The baby was intubated and then transferred to our Neonatal Intensive Care Unit (NICU) at "San Salvatore" Hospital, L'Aquila, at five hours of life.

In our NICU the blood exams revealed an Hb of 5.3 g/dl with an Ht of 17.5%, RBC count $1.53 \times 10^6/mm^3$ and erythropoietin (EPO) 103 mIU/ml (normal value [nv]: 2.50-35 mIU/ml).

At about nine hours of life an exchange transfusion (ET) was started and stopped when the Ht level was 50%. Inotropic support with dopamine and dobutamine was started. Blood exams post-ET showed: Hb 13.7 g/dl, Ht 44.4% and RBC count $4.13 \times 10^6/mm^3$. Adverse events post-ET were hypocalcemia treated with intravenous calcium for two days and thrombocytopenia (platelets 57,000/mmc^3) resolved after four days.

On day 1 of life echocardiogram revealed mild persistent pulmonary artery pressure at 35 mmHg and cranial ultrasound was normal.

On day 6 of life neonate's blood exams showed: Hb 13.7 g/dl, Ht 44.7%, RBC count $4.29 \times 10^6/mm^3$, reticulocytes 1.45%, platelets 183,000/mmc^3, EPO 103 mIU/ml (nv: 2.50-35 mIU/ml).

Flow cytometry test revealed a FMH of approximately 5.70 ml of fetal red cells (nv < 0.22 ml).

She was discharged on day of life 14 in good condition.

Case report 2

A baby girl, weighing 2.080 kg, small for gestational age (SGA), was born at $37^{5/7}$ gestational weeks by emergent cesarean delivery for recurrent fetal decelerations in a second level hospital. The pregnancy had been complicated by intrauterine growth retardation (IUGR). TORCH and scans during pregnancy were negative.

At birth the infant appeared pale, floppy with no initial respiratory effort and was ventilated. The Apgar scores were 7 at 1 minute and 8 at 5 minutes.

At one hour of life the arterial blood gas showed respiratory acidosis and anemia (Hb 7.5 g/dl, Ht 23%).

At four hours of life the neonate was transferred to our NICU at "San Salvatore" Hospital, L'Aquila, for further evaluation and management. On admission her vital parameters were: temperature

36.1°C, heart rate 110 beats/min (bpm), respiratory rate 40/minute, SpO_2 85-88% with FiO_2 1 and normal blood pressure. Physical exam revealed a very pale infant, no evidence of peripheral edema or hydrops, spontaneous respiratory effort with an elevated need of oxygen, heart murmur and hepatosplenomegaly.

The initial data were: Hb 8 g/dl, Ht 25.1%, RBC 2.13 x 10^6/mm^3, reticulocytes 6.85%, EPO 3,750 mIU/ml (nv: 2.50-35 mIU/ml) and total bilirubin 3.11 mg/dl. One packed red cells transfusion of 20 ml/kg was required.

A sepsis evaluation and empiric antibiotics were started. Blood culture, urine CMV-DNA PCR and Parvovirus B19 antibodies were negative.

Cranial ultrasound showed mild-moderate frontal and basal ganglia hyperechogenicity.

At six hours of life the baby deteriorated and required intensive cardio-respiratory support with O_2 100% (SpO_2 60%).

Adrenaline and inotropic support (dopamine and dobutamine), boluses of saline (10 ml/kg) as well as packed red blood transfusion were given without any improvement in clinical condition.

In spite of expansive supportive measures being taken the baby's conditions continued to deteriorate and the baby expired at seven hours of life.

Flow citometry test revealed an FMH of approximately 40 ml of fetal red cells (nv < 0.22 ml).

Case report 3

A gravida 0 para 0 woman presented to the delivery room at "San Salvatore" Hospital, L'Aquila, at $39^{4/7}$ gestational weeks. Her prenatal laboratories and scans were unremarkable. Current pregnancy was uneventful. Rupture of membranes occurred at delivery, with clear amniotic fluid.

A baby boy, weighing 3.320 kg (AGA), was born by emergency cesarean for recurrent variable fetal heart rate decelerations. Apgar score were 8 at 1 minute and 9 at 5 minutes.

The mother's blood type was A negative and infant's blood type was A positive, Kell-positive with direct Coombs test negative.

Few minutes after birth the infant appeared very pale and floppy and he was rapidly transferred to NICU. Fetal acidemia (pH 7.20; ABE -12 mmol/L; HCO_3 18 mmol/L) was noted and confirmed at one hour of life (pH 7.20; ABE -16 mmol/L; HCO_3 11.7 mmol/L).

During the first four hours of life the baby showed a progressive need of oxygen (SpO_2 88-90% with FiO_2 0.4, heart rate 125 bpm). Hypotension (mean blood pressure 39 mmHg) was treated initially by a bolus of normal saline and then inotropic drugs.

The blood exams revealed severe anemia with Hb 3.8 g/dl, Ht 15.5%, RBC 1.25 x 10^6/mm^3, reticulocytes 12.7% and EPO 33,000 mIU/ml (nv: 2.50-35 mIU/ml) treated by ET until the Ht level was 36%.

At six hours of life the baby showed progressive respiratory distress and mechanical ventilation was necessary. Pulmonary hypertension treated with sildenafil for six days and temporary ventricular hypokinesia were diagnosed by echocardiogram.

A sepsis evaluation and empiric antibiotics were started. Blood culture, urine CMV-DNA PCR, Parvovirus B19 PCR and EBV antibodies were negative. Serial cerebral scans and MRI were performed and resulted normal.

After positive fetal bleed screens via Rosette testing, flow cytometric analysis was performed to quantify the volume of hemorrhage and revealed an FMH of approximately 83.4 ml of fetal red cells (nv < 0.22 ml).

Considering the result of the flow cytometry test and the Rh incompatibility, in the immediate post-partum period, Rh prophylaxis with 7 doses of Rh-Immunoglobulin (RhIG) was administrated to the mother to minimize the risk of alloimmunization in D-negative mothers of D-positive newborn.

The baby was discharged on day of life 14 in good condition.

Case report 4

A 35-years-old gravida 0 para 0 presented to the delivery room at "San Salvatore" Hospital, L'Aquila, at $37^{5/7}$ gestational weeks. The pregnancy was uncomplicated, all prenatal laboratories and scans were unremarkable. Spontaneous rupture of membranes occurred > 24 hours. Vaginal colonization with Group B streptococcus was negative. A baby boy, weighing 2.800 kg (AGA), was born by vaginally delivery with clear amniotic fluid.

At birth the infant appeared very pale, floppy with respiratory depression and required intensive resuscitation, including intubation, PPV and need of oxygen until FiO_2 0.5. Poor perfusion and tachycardia (heart rate 180 bpm) were also noted so two bolus of normal saline (10 ml/kg) were

administered intravenous. Apgar scores were 1, 5 and 7 at 1, 5 and 10 minutes, respectively. The baby was rapidly transferred to NICU.

The mother's and infant's blood types were 0 positive and 0 negative respectively with direct Coombs test negative.

Fetal acidemia (pH 7.10; ABE -11 mmol/L; HCO_3 18.8 mmol/L) was noted and confirmed (pH 7.21; ABE -20 mmol/L; HCO_3 7.9 mmol/L) and corrected at about one hour of life.

On admission in NICU his vital signs were: SpO_2 99% with FiO_2 0.35 in mechanical ventilation, heart rate 155 bpm, mean blood pressure 35 mmHg. The initial data were: Hb 13.5 g/dl, Ht 41.8% and RBC 3.75 x 10^6/mm^3.

Hypotension was treated by a third bolus of normal saline and then by positive inotropic drugs (dopamine and dobutamine).

Mechanical ventilation was stopped at four hours of life and the baby needed supplemental oxygen (FiO_2 0.25) for other twelve hours. The infant was still pale and the blood exams showed an anemia with Hb 11.4 g/dl, Ht 35.7% and RBC 3.25 x 10^6/mm^3 and deranged coagulation corrected with a transfusion of fresh frozen plasma.

At about twelve hours of life the complete blood count showed a rapid blood loss with an Hb of 9.3 g/dl with Ht of 27.9%, RBC 2.63 x 10^6/mm^3, reticulocytes 2.9%, EPO 8.59 mIU/ml (nv: 2.50-35 mIU/ml) therefore a transfusion of 0-negative packed RBCs (15 ml/kg) was performed. The post-transfusion Ht was 48%.

A sepsis evaluation and empiric antibiotics were started. Blood culture, Parvovirus B19 antibodies and TORCH titers were negative.

Cerebral function monitoring (aEEG), electroencephalogram, serial cerebral scan and MRI resulted normal.

Flow cytometry test revealed an FMH of approximately 69.36 ml of fetal red cells (nv < 0.22 ml).

He was discharged on day of life 11 in good condition.

Case report 5

A 28-year-old gravida 3 para 2 presented to the delivery room in a second level hospital at 37 $^{5/7}$ gestational weeks for the beginning of labour. Her prenatal scans and laboratories were unremarkable. Current pregnancy was uneventful.

A baby boy, weighing 2.800 kg (AGA), was born by emergent cesarean delivery because the mother had precedent cesarean section. The amniotic fluid was stained by meconium.

The Apgar scores were 9 and 10 at 1 and 5 minutes, respectively.

The mother's and infant's blood types were B positive and 0 positive respectively with direct Coombs test negative.

At birth the newborn was well. In the first day of life he was noted to be pale and a complete blood count showed an Hb of 8.5 g/dl with an Ht of 27.6% and RBC count 2.45 x 10^6/mm^3.

At 17 hours of life he was transferred to our NICU at "San Salvatore" Hospital, L'Aquila.

On admission his vital parameters were: temperature 36.2°C, heart rate 134 bpm, respiratory rate 40/minute, SpO_2 100% in air room and mean blood pressure 42 mmHg.

The initial data were: Hb 7.6 g/dl, Ht 27.9%, RBC count 2.39 x 10^6/mm^3 and EPO 354 mIU/ml (nv: 2.50-35 mIU/ml). One packed red cells transfusion of 20 ml/kg was performed.

Hypocalcemia (7.5 mg/dl) was noted and promptly corrected. Echocardiogram revealed a membranous ventricular septal defect with left-right shunt; abdomen and cerebral scans were normal.

Blood exams post transfusion showed: Hb 15.1 g/dl, Ht 47% and RBC count 4.88 x 10^6/mm^3.

Flow cytometry test revealed an FMH of approximately 94.74 ml of fetal red cells (nv < 0.22 ml).

He was discharged on day of life 8 in good condition.

Discussion

FMH can begin any time from the mid-first trimester onwards.

There is no universally accepted definition of the degree of fetal erythrocyte transfer that constitutes FMH, but a wide range of blood volumes between 10 and 150 ml have been proposed. Thresholds of 80 ml or 150 ml also have been proposed to define "large" or "massive" fetomaternal bleeds and the incidence of FMH was 0.9 and 0.2 per 1,000 births respectively [4].

Given the ambiguity of the definition of a clinically relevant volume of hemorrhage it is clear that more factors are important: the rate of blood loss, the chronicity of the bleed and the gestational age.

The etiology of FMH is varied: fetal factors (malformation, twin-to-twin transfusion, mono-

amniotic monochorionic twins, fetal death); placental abnormalities (placenta previa, abruption, tumors, umbilical vein thrombosis); maternal trauma; obstetrical interventions (amniocentesis, cordocentesis) and other factors for example hypertension and substance abuse (cocaine). However more than 80% of cases in which the FMH is estimated to be greater than 30 ml remain unexplained [10]. Massive FMH has a wide spectrum of clinical presentations depending on the volume of the hemorrhage and the rapidity with which it occurred. Often FMH occurs without an evident precipitating factor. Clinical finding associated with FMH were neonatal anemia, stillbirth, IUGR, hydrops fetalis, decreased or absent fetal movements, non-reassuring fetal heart rate tracing, sinusoidal fetal tracing, and fetal tachyarrythmias [9].

When an infant is born with unexpected anemia, in addition to FMH, physicians should consider alternative diagnoses such as isoimmune hemolytic anemia (Rh incompatibility) or autoimmune causes, congenital infections that result in bone marrow suppression (TORCH) or bacterial sepsis, congenital erythrocyte defects of structure (spherocytes) or function (G6PD; pyruvate kinase deficiency), congenital hemoglobinopathies (α-thalassemia) or congenital hypoplastic anemia (Diamond-Blackfan syndrome) [11].

Unfortunately, the determination of the timing of FMH is difficult to ascertain. Instead, clinical and laboratory parameters are utilized to assess the chronicity of FMH. Previously *in utero* diagnosis has been described as a classic triade including: decreased or absent fetal movements, sinusoidal heart rate pattern and hydrops fetalis. Giacoia observed that sinusoidal fetal heart rate pattern occurred in only 10% of FMH cases and currently decrease or absence of fetal movements are considered the most common antenatal presentation of FMH [8].

In acute FMH, rapid fetal blood loss is associated in uterus with non-reassuring fetal heart rate patterns, IUGR and fetal anemia while after birth we can observe perinatal hypoxia or acidemia, immediate hemodynamic neonatal instability and even stillbirth or neonatal death.

In the event of massive fetal blood loss, the mother may experience a transfusion reaction expressed as nausea, edema, fever and chills.

In cases of chronic FMH, the fetus reacts by hemodynamic compensatory mechanisms of enhanced hemopoietic activity (increased production of erythrocyte precursors such as erythroblasts, reticulocytes and nucleated RBC) [9]. If the fetus can compensate for the blood loss, the pregnancy may continue and the infant will present with varying degrees of anemia. Initially, the fetus may increase cardiac output with fetal tachycardia [12]. Vascular redistribution of fetal blood flow occurs with increased shunting of blood away from the somatic circulation to the brain, heart and adrenal glands. The vascular alterations are often referred to as the brain-sparing effect and may be documented sonographically as diminished resistance indices and increased diastolic velocities in the middle cerebral artery (MCA) [13]. Ultrasonographic evaluation for the presence of hydrops fetalis as well as the MCA peak systolic velocity (MCA PSV) should also be performed. MCA PSV values of greater than 1.5 multiples of the median (MOM) suggest possible fetal anemia [14]. In the setting of uncompensated anemia, the fetus may develop high-output heart failure and hydrops fetalis [15]. After birth, a chronic blood loss can involve severe anemia with higher reticulocyte count and EPO causing birth asphyxia, acidemia and neonatal death. There are some inexplicable cases in which massive FMH are clinically silent and further investigation are necessary.

Several diagnostic modalities for FMH have been described:

1. Kleihauer-Betke test, based on the principle that fetal hemoglobin (HbF) is resistant to acid elution compared to adult hemoglobins, identifies fetal RBC in maternal blood after immersion in acid solution, resulting in differential staining: erythrocytes containing HbF appear red while maternal RBC are not stable after the acid treatment and don't take-up the stain, appearing as ghost cells on the slide. This test is rapid but semi-quantitative and liable to false positive results.
2. Flow cytometry can identify cells by size (fetal cells are larger than maternal cells) [16] and fetal cells tagged with monoclonal antibodies [17] in maternal blood sample. The analysis for D-Antigen can be used in place of or in addition to HbF.
3. Rosette test is a qualitative screening test that indirectly identifies Rh-positive blood in Rh-negative mothers [17]. Even if this test is positive a quantitative test is required.

In the uncommon event that fetal anemia is recognized before delivery, the risk and benefit of

immediate delivery should be evaluated. If the infant is near-term gestation, immediate cesarean delivery is indicated considering that the compromised placenta may not support the stress of labor [18]. If the fetus is still of preterm gestation, *in utero* transfusion can be considered to safely temporize the effect of fetal anemia [19, 20].

After birth, if anemia is present, it should be corrected slowly to avoid volume overload and exacerbation of heart failure. In cases with the most profound anemia, ET may allow for rapid correction of the anemia [21, 22]. If the child's condition is unstable, packed red cells may be more readily available [23].

The outcome of infants with FMH may depend on the size of the hemorrhage in relation to the overall fetal blood volume, the rate at which this blood is lost, and whether the event is acute or chronic. The prognosis for fetuses is variable. Massive or untreated anemia can result in cardiac failure, hydrops, hypovolemic shock, intrauterine and neonatal death, neurologic injury, cerebral palsy or persistent pulmonary hypertension [24].

In the literature single cases and small case series are reported [25-31] and short-term outcomes of FMH infants analysed [6, 7].

Neonatal concentration of Hb is a significant prognostic index for short- [6, 7] and long-term [4, 10] outcome [1]. In a study of 16 infants with ≥ 20 ml, short-term outcome was poor in 5/7 with Hb < 4 g/dl, while none of 9 infants with Hb > 4 g/dl had adverse outcomes. In another study of short-term outcomes, adverse events, including intraventricular hemorrhage and periveritricular leukomalacia, occurred in 4/11 (36%) with Hb < 4.5 g/dl, while in none of the 13 infants with Hb > 4.5 g/dl [7]. In a study examining a long-term outcome in 31 FMH infants with neonatal Hb 4.8-15.4 g/dl, none developed neurological sequelae. In another study, in 12 surviving FMH with neonatal Hb of 2.4-14 g/dl, 2/4 infants with Hb < 4.5 g/dl had poor outcomes, while none of the 8 with initial Hb > 4.5 g/dl developed neurological sequelae.

Our five cases of FMH had characteristics evoking both acute and chronic anemia (**Tab.1**).

The pregnancies were uneventful except in the second case, complicated with IUGR.

In the first three cases an emergent cesarean delivery was performed for recurrent fetal decelerations and in the fifth case for the beginning of labour in a mother with a precedent cesarean section.

The infants presented with many of the classical signs and symptoms associated with FMH.

Table 1. Hematological parameters.

	Hb (g/dl)	Ht (%)	EPO (mIU/ml)	FMH (ml)
Case 1	2.8	9.7	103	5.70
Case 2	7.5	23	3,750	40
Case 3	3.8	15.5	33,000	83.4
Case 4	9.3	27.9	8.59	69.36
Case 5	8.5	27.6	354	97.74

Hb: hemoglobin; Ht: hematocrit; EPO: erythropoietin; FMH: fetomaternal hemorrhage.

Except the last case, at birth the infants were immediately recognized to be pale, with poor perfusion and had a severe metabolic acidosis. They were supported by inotropic drugs and treated with mechanical ventilation for severe respiratory distress.

In the first case the baby was born in a first level unit and the initial level of Hb was 2.8 g/dl. She was treated immediately with a packed red blood transfusion. In our NICU an ET was started at a level of Hb of 5.3 g/dl (Ht 17.5%) and stopped when the Ht was 50%.

In the second case the initial level of Hb was 7.5 g/dl and the baby was transferred to our NICU after four hours of life. Anemia with higher reticulocyte count and EPO was suggestive of chronicity or *in utero* bleeding. The baby progressively deteriorated although intensive resuscitation and packed red blood transfusion and expired at seven hours of life. The final impression was chronic FMH leading to severe anemia causing birth asphyxia and neonatal death.

In the third case the most profound anemia (Hb 3.8 g/dl) was slowly corrected by ET to avoid volume overload and exacerbation of heart failure. In this case the degree of FMH is probably underestimated for maternal incompatibility and isoimmunization since the fetal blood cells that enter the maternal circulation are rapidly cleared by the maternal reticuloendothelial system.

In the fourth case the baby needed immediate resuscitation at birth. In the first twelve hours of life there was a rapid blood loss and the level of Hb dropped from 11.4 g/dl to 9.3 g/dl so an immediate packed red blood transfusion was performed. Furthermore the deranged coagulation can be explained as result of the severe degree of birth asphyxia.

In the fifth case the baby was born in a second level unit and the initial level of Hb was 8.5 g/dl. The baby was transferred to our NICU after

seventeen hours of life. Anemia with higher EPO level was suggestive of chronicity or *in utero* bleeding. A red blood transfusion was started at a level of Hb of 7.6 g/dl (Ht 27.9%). According with a study of a short-term outcomes [6], the baby was always well in spite of the level of Hb 8.5 g/dl and the highest passage of fetal red cells revealed with the flow cytometry test.

Conclusion

It's our hope that our experience can assist practitioners in the management of FMH.

It's important considering that, in a first level unit, it's safe to consider a blood transfusion waiting to transfer the baby in a NICU.

In cases of FMH it's very important to obtain rapidly an accurate measurements of fetal blood losses via flow cytometric analysis, especially in clinically-unsuspected cases when it's necessary a prompt administration of adequate immunoprophylaxis to D-negative mothers.

The entity of massive FMHs, particularly those that are clinically silent, warrants further investigation.

In case of neonatal anemia, the physician's awareness of the condition, the ability to suspect and diagnose FMH with appropriate testing on the postpartum mother have a significant impact on the epidemiology, accurate management and prognosis for the anemic neonates [32].

Practice points

- FMH may be a significant cause of neonatal anemia.
- Determination of the timing of FMH is difficult to ascertain and there are clinical and laboratory parameters utilized to assess the chronicity of FMH.
- Appropriate testing on the postpartum mother are indispensable.
- Diagnosis of FMH and prognosis for anemic neonates and their families are highly dependent on physician awareness of the condition.
- Red blood transfusion is recommended, while in case with severe anemia and cardiac failure an ET can be considered.

Abbreviations

ABE: acid base excess
AGA: adequate for gestational age
EPO: erythropoietin
ET: exchange transfusion
FMH: fetomaternal hemorrhage
Hb: hemoglobin level
HbF: fetal hemoglobin
Ht: hematocrit
IUGR: intrauterine growth retardation
MCA: middle cerebral artery
MCA PSV: MCA peak systolic velocity
MOM: multiples of the median
NICU: Neonatal Intensive Care Unit
nv: normal value
PPV: positive pressure ventilation
RhIG: Rh-Immunoglobulin
RBC: red blood cell
SGA: small for gestational age

Declaration of interest

The Authors declare that there is no conflict of interest.

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