ANALYSIS

24(101), January - February, 2020

ISSN 2321–7359 EISSN 2321–7367

Medical Science

Neonatal Outcomes of Rh Alloimmunization Pregnancy Treated with Intrauterine Transfusion

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Article History
Received: 19 August 2019
Reviewed: 20/August/2019 *to* 8/October/2019
Accepted: 11 October 2019
Prepared: 14 October 2019
Published: January - February 2020

Citation
Shirin Niroomanesh, Salmeh Dadgar, Mahboobeh Shirazi, Fatemeh Rahimi Sharbaf, Fatemeh Golshahi. Neonatal Outcomes of Rh Alloimmunization Pregnancy Treated with Intrauterine Transfusion. *Medical Science*, 2020, 24(101), 57-65

ABSTRACT

Introduction: Fetal anemia is a major problem and cause of neonatal morbidities and mortalities. Maternal Rh allo-immunization has not been eliminated with subsequent erythroblastosis fetalis and hemolytic disease still occasionally occurring. In this study, we evaluated the neonatal outcomes of intra-uterine transfusion (IUT)-treated pregnancies because Rh allo-immunization and fetal anemia. *Patients and Methods:* This was a prospective cohort study in which we evaluated pregnancies between 17-35 week gestational ages in Rhesus negative mothers who referred to perinatology clinic because of fetal anemia, Tehran University of Medical Sciences during May 2016 to April 2018 in Yas Hospital. Anemia was confirmed by Doppler ultrasonography. For all patients, intra-uterine transfusion was performed based on gestational age. Demographic, clinical and para-clinical variables were measured in each case and each time of IUT. *Results:* There were 33 Rh iso-immunized pregnancies; of which 6 fetuses were hydropic and remaining 27 were non-hydropic. IUT was perfumed 86 times in these cases. The mean of mother age was 31.24± 6.06 years old. The mean hemoglobin after birth was 7.92± 2.65 g/dL. The mean of transfused blood in all cases was 92.73± 45.14 cc. The survival rate in our study was 75.8% and eight fetuses were died (24.2%). There were significant difference between ACA PSV (P=0.012) and MCA PSV (P=0.015) with neonatal outcome (mortality or survival) in our study. *Conclusion:* In our investigation, IUT was shown to be lifesaving and very effective in the management of Rh immunized pregnancies. The results were comparable with other evaluations with high survival rate. We also showed that both ACA PSV and PCA PSV have a same value in diagnosis of fetal anemia. MCA PSV and ACA PSV can significantly predict the mortality of fetus after IUT.

Keywords: Rh immunization, Intra-uterine transfusion, fetal Doppler sonography

1. INTRODUCTION

Fetal anemia is a major problem and cause of neonatal morbidities and mortalities. Fetal anemia can be detected reliably by noninvasive measurements of the Middle Cerebral Artery Peak Systolic Velocity (MCA-PSV). The value in anemia is MCA-PSV>1.5 MoM (Oepkes, Seaward et al. 2006). Rodeck et al. performed the first Intrauterine Blood Transfusion (IUT) using the intraperitoneal technique. In the 1980s, this technique was replaced by intravascular IUT (Rodeck, Holman et al. 1981). This procedure is currently performed through single or repeated direct intravascular injections of red blood cells from an Rh-negative donor through the intrahepatic umbilical vein or the umbilical cord at its placental insertion (Oepkes and van Scheltema 2007). Although the use of anti-D prophylaxis has dramatically reduced the need for IUT, the procedure continues to be an essential modality for the treatment of severe fetal anemia from a variety of causes (Rodeck, Holman et al. 1981). Because of improvements in obstetric and neonatal management, the perinatal survival rate for babies treated with IUT for alloimmune fetal anemia exceeds 90% (Oepkes and van Scheltema 2007). This improved survival rate has resulted in increased attention to the short- and long-term outcomes in surviving children. Information regarding the adverse effects of IUT on detailed neonatal outcome is limited (Altunyurt, Okyay et al. 2012). Outcomes have been reported to be dependent on many factors, including the primary cause and severity of fetal anemia, the severity and reversibility of hydrops at the time of diagnosis, and the time when the therapy was initiated (van Kamp, Klumper et al. 2001, Van Kamp, Klumper et al. 2004, Lindenburg, Smits-Wintjens et al. 2012). Long-term follow up studies have revealed normal neurologic outcomes in 95% of cases (Lindenburg, Smits-Wintjens et al. 2012).

While the use of elevated middle cerebral artery peaks systolic velocity (MCA PSV) in assessing fetal anemia is well known, its occurrence is uncommon due to the current practice of giving prophylactic doses of ultrafiltered Rh (D) immunoglobulin (anti-D) in Rh (D) negative women. There are limited investigations on ACA and PCA variables in this field. In mothers who do not receive prophylaxis with Rh immunoglobulin, the overall risk of -immunization for an Rh-positive ABO-compatible infant with an Rh-negative mother is about 16% (Lee and Nasser 2010). With appropriate use of anti-D the incidence of fetal anemia is approximately 0.1% of pregnancies in Rh (D) negative women (Moise, Lockwood et al. 2009). Despite this, maternal Rh allo-immunization has not been eliminated with subsequent erythroblastosis fetalis and hemolytic disease still occasionally occurring. In this study, we evaluated the neonatal outcomes of intra-uterine transfusion (IUT)-treated pregnancies because Rh allo-immunization and fetal anemia and comparison of Doppler of three arteries (MCA, ACA and PCA).

2. MATERIALS AND METHODS

This was a prospective cohort study. We evaluated pregnancies between 17-35 week gestations age in Rhesus negative mothers who referred to perinatology clinic due to fetal anemia and receiving intra-uterine transfusion, Tehran University of Medical Sciences during May 2016 to April 2018 in Yas Hospital.

Study population

Pregnant women with gestational age between 17 to 35 weeks, with below characteristics were included in the study:
Maternal negative Rhesus
Maternal positive indirect coombs test
Fetal anemia (confirmed by MCA PSV>1.5 Mom)
No fetal anomaly according to anomaly ultrasonography
Single tone pregnancy
We excluded patients who had no consent for participation and history of underlying diseases. Patients received erythropoietin was excluded from the study.

Study design

Pregnant women were enrolled in the study after obtaining informed consent. We calculated gestational age based on first trimester ultrasonography. The diagnosis of fetal anemia was performed by Doppler sonography and middle cerebral artery (MCA) peak systolic velocity (PSV). For exact evaluation and comparing the results with MCA, primatologist with more than 5 years experience investigated anterior cerebral artery and posterior cerebral artery Doppler sonography

Ultrasound

Axial section of brain, including thalami, cavita sep, ti pellucidi was obtained and the circle of Willis was identified. The MCA, PCA and ACA nearest to US probe were identified, Doppler US switched on and the peak systolic velocity measured carefully.

Procedures

If MCV PSV were more than 1.5 MoM (Multiple of the Median), patients had indication to intra-uterine transfusion. Before starting IUT, blood samples of fetuses were sent for hemoglobin level and other tests for all patients. We also consider the sonographic presentation of fetal hydrops as an indication of sampling from fetal blood. Fetuses with lower than two standard deviations of the mean in the same pregnancy consider as anemic. After admission of patients, biometric sonography was performed for seeking hydrops, weight of fetus and the location of placenta. Doppler of MCA, ACA and PCA was performed, too. All patients' fetus blood samples were assessed for antibody screening, complete blood count and in the first IUT, the level of bilirubin; reticulocyte, hemoglobin and direct coombs measured and after IUT blood sample were obtained for transfusion sufficiency. In mothers between 24-34 weeks of gestational age, we administered two doses of betamethasone with 24 hours interval 48 hours before IUT in order to lower the risk need to urgent cesarean. Patients had 6-8 hours fasting before the operation. Atracurium 0.4 mg/kg was used for all fetuses. All babies and their mothers were treated by the same staff physicians and underwent standard follow-up examinations.

Table 1 hemoglobin and hematocrit levels

Target hematocrit minus beginning hematocrit = Desired increment in hematocrit	Transfusion coefficient
10	0.02
15	0.03
20	0.04
25	0.05
30	0.06

Intra-uterine transfusion

IUT was performed by the following techniques:

Intra vascular transfusion (IVT) was tried first especially if the fetus was hyropic. Volume of blood transfused was quickly calculated after the first cord blood sampling for hemoglobin and hematocrit levels as Table 1.

Intra-peritoneal transfusion (IPT)

If approach to cord was difficult due to different causes such as posterior placenta, obesity and fetal ascites, early gestation, IPT was performed.

Ethics

All participant mothers received complete information on the purpose of the study. Informed consent was obtained from each baby's guardian after approval of the study protocol by the institutional human ethical committee and the deanship of scientific research at the University of Tehran (Ethical code: IR.TUMS.MEDICINE.REC.1397.415). This study was conducted according to principles of the Helsinki Declaration.

Definitions

Gestational Age (GA) was determined according to the fetal ultrasound in the first trimester. Severe fetal anemia was defined as a cord blood hemoglobin level of less than 5.5 gm/dl and an MCA-PSV<0.55 multiples of the median for a given GA. Non severe fetal anemia (mild to moderate) was defined as a cord blood Hb level between 5.5 and 10 gm/dl and an MCA-PSV<0.84 multiples of the median (mild) or <0.65 multiples of the median (moderate) for a given GA. Hydrops was defined as the presence of accumulated fluid in at least one fetal body cavity (mainly ascites), along with fetal skin edema. Patients were undergoing again IUT according to gestational age, first hemoglobin and volume of transfused blood.

Planned delivery was defined as a planned elective cesarean section without labor or a planned induced vaginal delivery or cesarean section due to failed planned induction. Unplanned delivery was defined as spontaneous vaginal delivery or urgent cesarean section due to maternal or fetal causes. Phototherapy, Intravenous Immune Globulin (IVIG), and exchange transfusion were performed according to the American Academy of Pediatrics guidelines.

Fetal characteristics

The following fetal data were recorded: GA at which IUTs were administered, number of IUTs, fetal Hemoglobin concentration (HB/hematocrit) as diagnosed by MCA-PSV and cordocentesis before and after IUT, severity of fetal anemia, and evidence of ascites and hydrops.

Neonatal outcomes

Delivery room: Data were collected on the immediate delivery outcome, including mode of delivery, birth weight, gender, GA, and baby condition at birth, including the death or live.

Procedure of IUT fetal transfusion

There are two methods to perform fetal blood transfusions: Intravascular transfusion (IVT): blood is transfused into the umbilical cord; Intraperitoneal transfusion (IPT): blood is transfused into the fetus' abdomen. The mother is given antibiotics, local anesthesia and IV sedation, which also sedates the fetus. The fetus may be given additional medication to stop movement. Using ultrasound to determine the position of the fetus and placenta, the surgeon inserts a needle into the mother's abdomen and then into the umbilical cord vein or the fetus' abdomen. Red blood cells that are compatible with the fetus' blood type are passed through the needle into the fetus.

Ultrasound and color Doppler was first done for fetal heart activity, and placental site. Access site and needle path were mapped with plan to enter the cord at cord insertion or free loop. Fetus was paralyzed using Vecuronium IM/IV 0.3 mgm/kg fetal weight into fetal buttock or umbilical vein, if fetal movements were excessive or placenta was posterior. A 20 gauge long needle was inserted under continuous U/S guidance by free hand technique. Needle tip was inserted with a sharp jerk into the umbilical vein; the stillete withdrawn, syringe attached and 2-3 ml blood aspirated and sent for laboratory values. In IPT, the needle was inserted into the fetal peritoneal cavity.

Packed RBC was the transfused by pushing the required volume with a 10-20 cc syringe at the rate of about 10ml/min. After the transfusion in IVT, blood for post transfusion hematocrit was aspirated. Fetal heart activity was checked intermittently throughout the procedure for tachycardia, bradycardia or other complications.

Sample size

The rate if allo-immunization is generally 2%. The prevalence of this feature is about 0.038% in Iran. Our sample size was defined with 95% confidence interval by below formula:

$n= Z^2 \times P\ (1-P)/d^2 = (1.96)^2 \times 0.00038 \times 0.99963/ (0.01)^2 = 14.59 \approx 15$

Statistics

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, version 19). Maternal and neonatal characteristics and outcomes were examined, and data are presented as raw frequencies. A P-value of less than 0.05 was regarded as statistically significant.

3. RESULTS

There were 33 Rh iso-immunized pregnancies; of which 6 fetuses were hydropic and remaining 27 were non-hydropic. IUT was perfumed 86 times in these cases. Most of the patients had a history of affected pregnancies (Table 2). The mean body mass index (BMI) of mothers was 27.95± 3.86 and the mean of mother age was 31.24± 6.06 years old. The mean gestation age at first IUT was 27.61± 3.93 weeks. Three of cases (9.1%) were nulliparous and 90.9% of them were multi-parous. Table 3 shows the baseline characteristics of the study population. Figure 1 shows the pattern of blood group and Rh in mother and neonates in our study population.

Table 2 The baseline characteristics in hydropic and non-hydropic patients

Characteristics	Hydropic	Non-hydropic	P value
Age (mean± S.D) years	31.33± 5.89	31.16± 6.37	0.933
History of fetal death (n, %)	7, 21.2	19, 57.5	0.41
History of abortion (n, %)	5, 15.1	13, 39.3	0.28
Ascites (n, %)	13, 86.7	3, 16.7	0.001

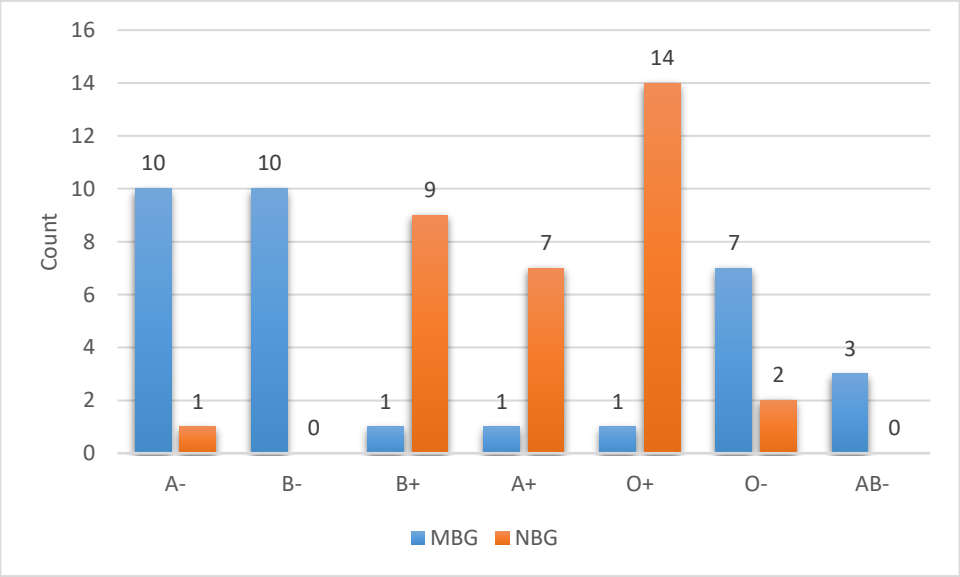

Figure 1 The pattern of blood group and Rh in study population

Table 3 Baseline characteristics

Variable		
The amount of transfused blood	<30 cc (n, %)	7, 8.1
	30-50 cc (n, %)	10, 11.6
	50-100 cc (n, %)	37, 43
	100-150 cc (n, %)	23, 26.7
	>150 cc (n, %)	9, 10.5
Mean transfused blood in all 86 time IUTs (mean± S.D) cc	92.73± 45.14	
Gestation age (mean± S.D) weeks	28.72± 3.96	
Fetal weight in all 86 time IUTs (mean± S.D) gram	1299.39± 659.62	
Type of IUT (n, %)	Intravascular (25, 29,1), Intraperitoneal (61, 70.9)	
Serum Antibody (n, %)	Positive (28, 84.8), Negative (5, 15.2)	
Antibody titer (mean ± S.D)	0.0235± 0.0396	

MBG= maternal blood group and Rh; NBG= neonatal blood group and Rh.

The amount of transfused blood in our 33 cases (86 times) is listed in Table 3 beside other laboratory and underlying factors.

IUT= intra-uterine transfusion.

Laboratory, clinical and ultrasonographic findings is listed in Table 4.

Table 4 Laboratory, clinical and ultra-sonographic findings

Variable		
Number of IUT per case (n, %)	1	11, 33.3
	2	9, 27.3
	3	4, 12,1
	4	6, 18.2
	5	1, 3
	6	1, 3
	8	1, 3
Reticulocyte (mean± S.D) percent		3.33± 2.62
First Hemoglobin at IUT (mean± S.D) g/dL		7.92± 2.65
After IUT hemoglobin (mean± S.D) g/dL		13.65± 2.97
MCA PSV (mean± S.D)		46.90± 12.18
PCA PSV (mean± S.D)		48.81± 11.36
ACA PSV (mean± S.D)		45.06± 11.19
Period of Gestation at IUT (n, %)	<18 weeks	1, 1.2
	19-21	2, 2.3
	22-25	13, 15.1
	26-29	35, 40.7
	30-32	20, 23.7
	>33	15, 17.4

IUT= intra-uterine transfusion, **MCA= middle cerebral artery, PCA= posterior cerebral artery, ACA= anterior cerebral artery, PSV= peak systolic velocity.**

In our investigation, eight fetuses were died (24.2%) and others were alive (75.8%). Complications were reported in 10 cases (30.3%) including bradycardia and decrease of fetal heart rate. There was no relationship between parity of mother (P=0.578), history of abortion (P=0.064), history of death (P=0.0444), age (P=0.797) and mother BMI (P=0.982) with neonatal outcome. There was no correlation between fetal hydrops (P=0.541) and ascites (P=0.307) with neonatal outcome. There was no significant relationship between fetal weight (P=0.149), before IUT maternal hemoglobin (P=0.426), after IUT maternal hemoglobin (P=0.606), PCA (P=0.061), reticulocyte count (P=0.414), transfused blood volume (P=0.865).

Antibody titer was significantly higher in died fetuses rather than alive fetuses (P=0.023). There was negative significant correlation between positivity of coombs test before IUT with neonatal outcome (r=-0.353, P=0.044). There was significant difference

between ACA (P=0.012) and MCA (P=0.015) with neonatal outcome in our study (Table3). Delivery type was elective cesarean in 21 cases (84%) and urgent cesarean section in 4 cases (16%).

Surfactant was used in one case (3%). IVIG was used in two cases (6.1%). Auditory brain stem was done in 13 cases that showed normal pattern. In 9 cases exchange was performed (27.3%). Sixteen cases needed phototherapy (48.5%). The mean of final hemoglobin was 11.15± 2.91 g/dl. The mean of total transfused blood was 249.30± 138.91 cc. The mean duration of neonatal intensive care unit (NICU) was 16.96± 23.60 days.

IUT= intra-uterine transfusion, **MCA= middle cerebral artery, PCA= posterior cerebral artery, ACA= anterior cerebral artery, PSV= peak systolic velocity.**

There was significant correlation between results of MCA PSV with PCA PSV (r=0.874, P<0.001) and ACA PSV (r= 0.922, P<0.001). These correlations showed that both ACA PSV and PCA PSV have a same value in diagnosis of fetal anemia (Table 5).

Table 5 Clinical and para-clinic findings in different subgroups

Variable				P value
MCA PSV (mean± S.D)	Hydrops	yes	53.04± 7.67	0.006
		no	41.38± 8.63	
PCA PSV (mean± S.D)	Hydrops	yes	51.88± 8.59	0.074
		no	44.32± 8.72	
ACA PSV (mean± S.D)	Hydrops	yes	50.03± 7.82	0.021
		no	40.21± 9.02	
MCA PSV (mean± S.D)	Dead	yes	37.85± 2.61	0.015
		no	47.97± 9.98	
PCA PSV (mean± S.D)	Dead	yes	39.55± 3.46	0.061
		no	48.88± 9.28	
ACA PSV (mean± S.D)	Dead	yes	37.80± 1.69	0.012
		no	45.69± 9.89	

4. DISCUSSION

Despite the proven role of anti-D prophylaxis in decreasing the incidence of hemolytic diseases, maternal Rhesus type D isoimmunization still occurs (Zipursky, Bhutani et al. 2018). The unfavorable fetal and neonatal outcomes that were observed in this study could have been avoided by implementing preventive measures including a good screening program for maternal blood group, red-blood-cell antibody identification at the time of admission, and administration of anti-D prophylaxis at the appropriate time (Zipursky, Bhutani et al. 2018). Management of fetal anemia is not possible without ultra-sonographic monitoring and U/S guided intra-uterine fetal blood transfusion. It is however, a very difficult process requiring a lot of skill and precision, with a considerably high rate of procedure related feral death (Slootweg, Lindenburg et al. 2018). A variety of techniques such as exchange, partial exchange or simple top up transfusion via different sites such as percutaneous umbilical cord puncture at placental insertion or free loop, the intrahepatic umbilical vein or intraperitoneal transfusion have been employed.

The overall survival rate in our study was 75.8% (25 of 33 cases): 11 of the 15 hydropic fetuses (73.3%) and 14 of the non-hydropic fetuses were alive at birth and survived the perinatal period. It has been shown that in 44 ultrasound guided intravascular transfusion performed between 18 and 32 weeks on 15 patients with severe erythroblastosis fetalis due to Rh immunization, five transfusions were done in the intrahepatic umbilical vein, six were simple transfusions via percutaneous umbilical cord puncture and 33 were partial exchange. The overall rate was 67% (10 of 15 cases) with 4 of 8 hydropic and 6 of the 7 non-hydropic fetuses (Orsini, Pilu et al. 1988). In another series, of ultrasound guided feral intravascular transfusions in 78 fetuses, at Royal Women's Hospital all with severe erythroblastosis, a total of 288 intra-uterine transfusions were attempted with an overall survival rate of 75.6% (59 of 78) (Sampson, Permezel et al. 1994). The overall survival rate for delivered fetuses improved from 64.3% (18 of 28) in 1984-1987, to 82% (41 of 50) in 1988-1993. There was a total of 33 hydropic fetuses, of whom 20 (60.6%) survived, significantly fewer than non-hydropic fetuses (Vatsla, Deepika et al. 2010). Our results were in line with other studies reported by Altunyurt et al. (Badran, Al-lawama et al. 2013), Papantoniou et al. (Papantoniou, Sifakis et al. 2013) and Weisz et al. (Weisz, Rosenbaum et al. 2009) (73.5%, 83%_and 87%, respectively). Survival of neonates in our study was correlated with GA delivery (r=0.391, P=0.016) but not with GA at IUT (P=0.134), hydrops (P=0.388) and ascites (P=0.189). In Badran et al. study (Badran, Al-lawama et al. 2013), survival rate was not correlated with prenatal factors including the severity of fetal anemia, ascites, or hydrops; GA at first IUT; or GA at delivery. Altunyurt

et al. also indicated that there was no correlation between prenatal factors and survival rate (Altunyurt, Okyay et al. 2012). Higher survival rate in our study and similar study might be due to presence of good prognostic factors, including initiation of treatment after 20 weeks of gestation, Rh D negative status as the most common cause of fetal anemia, and reversal of all cases of fetal hydrops or ascites with adequate IUT treatment (van Kamp, Klumper et al. 2001, Van Kamp, Klumper et al. 2004, Snelgrove, D'Souza et al. 2019).

Intravascular transfusion is now believed to be more precise method for treating fetal anemia in erythroblastosis fetalis than is intra-peritoneal transfusion. Previously established guidelines for the volume of blood to be given in intravascular transfusion at a specific gestational age are not applicable for intravascular transfusion. In a study, 28 patients were underwent intravascular transfusion on 81 occasions between 19-34 gestational weeks (Cheong, Goodrick et al. 2001). The total number of transfusions ranged from one to six per patient. The aim at each procedure was to achieve a final hematocrit of 35-50%. Factors that determined the volume of blood required included pre-transfusion hematocrit, post-minus pre- transfusion hematocrit (hematocrit increase), the hematocrit of the transfused blood, gestational age, estimated fetal weight and interval from last transfusion. Intravascular as opposed to intraperitoneal transfusions were found to be the main method of transfusion in the later years in our study, a finding that was expected with improved sonographic equipment. Moreover, management and prognosis of anti-D red cell iso-immunization in pregnancy was found to have remained relatively stable since 1980s (Vatsla, Deepika et al. 2010).

In another study, it was reported that 67 intra-uterine transfusions carried out for 27 cases. Mean gestational age at first IUT was 27± 2.9 weeks. Of the 11 fetuses having gross ascites, eight were stillborn and two non-hydropic fetuses died. Two neonates died due to hemorrhagic disorder and prematurity, resulting in an overall survival rate of 55.6% (Gupte, Lulla et al. 1998). We showed that there was no significant association between a low reticulocyte count at birth and the number of IUTs which was in line with Altunyurt et al. (Altunyurt, Okyay et al. 2012) and Badran et al. (Badran, Al-lawama et al. 2013) and contrary to the previous studies conclusions (Farrant, Battin et al. 2001, De Boer, Zeestraten et al. 2008).

There are few centers in Iran, which are performing IUTs. Our results were comparable with standard centers in the world (van Kamp, Klumper et al. 2005, Oepkes and van Scheltema 2007). Our results demonstrated that there was significant correlation between results of MCA PSV with PCA PSV and ACA PSV and they can have same value in diagnosis of fetal anemia. Our study has some limitations; we did not follow the neonates for long-term outcomes, our sample size was small and the generalizability of the results is not enough.

5. CONCLUSIONS

In our investigation, IUT was shown to be lifesaving and very effective in the management of Rh immunized pregnancies. The results were comparable with other evaluations with high survival rate. We also showed that MCA and ACA PSV can related to survival rate of fetuses. Our results showed that both ACA PSV and PCA PSV have a same value in diagnosis of fetal anemia. More studies in our populations with large-scale sample size should be performed for seeking the diagnostic value of Doppler MCA or ACA PSV in predicting survival rate in IUTs. Early referral to equipped centers in fetal monitoring for early diagnosis of fetal anemia and IUT management is most important for optimal perinatal outcome.

Conflict of interest

There is no conflict of interest.

Acknowledgement

This study was supported by Tehran University of Medical Sciences financially.

REFERENCE

1. Altunyurt, S., E. Okyay, B. Saatli, T. Canbahishov, N. Demir and H. Ozkan (2012). "Neonatal outcome of fetuses receiving intrauterine transfusion for severe hydrops complicated by Rhesus hemolytic disease." International Journal of Gynecology & Obstetrics 117(2): 153-156.
2. Badran, E., M. Al-lawama, A. Masri, I. Al-Amouri and F. Kazaleh (2013). "Fetal intrauterine transfusion therapy: Neonatal outcomes." J Blood Lymph 3(112): 2.
3. Cheong, Y. C., J. Goodrick, P. M. Kyle and P. Soothill (2001). "Management of anti-Rhesus-D antibodies in pregnancy: a review from 1994 to 1998." Fetal diagnosis and therapy 16(5): 294-298.
4. De Boer, I. P., E. C. Zeestraten, E. Lopriore, I. L. Van Kamp, H. H. Kanhai and F. J. Walther (2008). "Pediatric outcome in Rhesus hemolytic disease treated with and without

intrauterine transfusion." American journal of obstetrics and gynecology 198(1): 54. e51-54. e54.
5. Farrant, B., M. Battin and A. Roberts (2001). "Outcome of infants receiving in-utero transfusions for haemolytic disease."
6. Gupte, S. C., C. Lulla, S. S. Kulkarni, S. A. Korgaonkar, V. Walvekar and R. Merchant (1998). "Experience with intrauterine transfusions for severe Rh alloimmunization in a developing country." The Journal of Maternal-Fetal Medicine 7(6): 287-291.
7. Lee, L. and J. Nasser (2010). "Doppler ultrasound assessment of fetal anaemia in an alloimmunised pregnancy." Australasian journal of ultrasound in medicine 13(4): 24.
8. Lindenburg, I. T., V. E. Smits-Wintjens, J. M. van Klink, E. Verduin, I. L. van Kamp, F. J. Walther, H. Schonewille, I. I. Doxiadis, H. H. Kanhai and J. M. van Lith (2012). "Long-term neurodevelopmental outcome after intrauterine transfusion for hemolytic disease of the fetus/newborn: the LOTUS study." American journal of obstetrics and gynecology 206(2): 141. e141-141. e148.
9. Moise, K., C. J. Lockwood and V. A. Barss (2009). "Pathogenesis and prenatal diagnosis of Rhesus (Rh) alloimmunization." Up To Date December 9.
10. Oepkes, D. and P. A. van Scheltema (2007). Intrauterine fetal transfusions in the management of fetal anemia and fetal thrombocytopenia. Seminars in Fetal and Neonatal Medicine, Elsevier.
11. Oepkes, D., P. G. Seaward, F. P. Vandenbussche, R. Windrim, J. Kingdom, J. Beyene, H. H. Kanhai, A. Ohlsson and G. Ryan (2006). "Doppler ultrasonography versus amniocentesis to predict fetal anemia." New England Journal of Medicine 355(2): 156-164.
12. Orsini, L. F., G. Pilu, P. Calderoni, S. Zucchini, N. Tripoli, M. C. Pittalis, L. Brondelli, S. Gabrielli, G. Sermasi and L. Bovicelli (1988). "Intravascular intrauterine transfusion for severe erythroblastosis fetalis using different techniques." Fetal Ther 3(1-2): 50-59.
13. Papantoniou, N., S. Sifakis and A. Antsaklis (2013). "Therapeutic management of fetal anemia: review of standard practice and alternative treatment options." Journal of perinatal medicine 41(1): 71-82.
14. Rodeck, C., C. Holman, J. Karnicki, J. Kemp, D. Whitmore and M. Austin (1981). "Direct intravascular fetal blood transfusion by fetoscopy in severe Rhesus isoimmunisation." The Lancet 317(8221): 625-627.
15. Sampson, A. J., M. Permezel, L. W. Doyle, L. de Crespigny, A. Ngu and H. Robinson (1994). "Ultrasound-guided fetal intravascular transfusions for severe erythroblastosis, 1984-1993." Aust N Z J Obstet Gynaecol 34(2): 125-130.
16. Slootweg, Y. M., I. T. Lindenburg, J. M. Koelewijn, I. L. Van Kamp, D. Oepkes and M. De Haas (2018). "Predicting anti-Kell-mediated hemolytic disease of the fetus and newborn: diagnostic accuracy of laboratory management." American journal of obstetrics and gynecology 219(4): 393. e391-393. e398.
17. Snelgrove, J. W., R. D'Souza, P. G. R. Seaward, R. Windrim, E. N. Kelly and G. Ryan (2019). "Predicting Intrauterine Transfusion Interval and Perinatal Outcomes in Alloimmunized Pregnancies: Time-to-Event Survival Analysis." Fetal diagnosis and therapy: 1-8.
18. van Kamp, I. L., F. J. Klumper, D. Oepkes, R. H. Meerman, S. A. Scherjon, F. P. Vandenbussche and H. H. Kanhai (2005). "Complications of intrauterine intravascular transfusion for fetal anemia due to maternal red-cell alloimmunization." American journal of obstetrics and gynecology 192(1): 171-177.
19. Van Kamp, I. L., F. J. Klumper, R. H. Meerman, D. Oepkes, S. A. Scherjon and H. H. Kanhai (2004). "Treatment of fetal anemia due to red-cell alloimmunization with intrauterine transfusions in the Netherlands, 1988–1999." Acta obstetricia et gynecologica Scandinavica 83(8): 731-737.
20. Van Kamp, I. L., F. J. Klumper, R. S. Bakkum, D. Oepkes, R. H. Meerman, S. A. Scherjon and H. H. Kanhai (2001). "The severity of immune fetal hydrops is predictive of fetal outcome after intrauterine treatment." American journal of obstetrics and gynecology 185(3): 668-673.
21. Vatsla, D., D. Deepika, G. Sumana, M. Suneeta, V. K. Paul and A. Deorari (2010). "Treatment of fetal anemia in Rh isoimmunized pregnancies with intrauterine fetal blood transfusion." The Journal of Obstetrics and Gynecology of India 60(2): 135-140.
22. Weisz, B., O. Rosenbaum, B. Chayen, R. Peltz, B. Feldman and S. Lipitz (2009). "Outcome of severely anaemic fetuses treated by intrauterine transfusions." Archives of Disease in Childhood-Fetal and Neonatal Edition 94(3): F201-F204.
23. Zipursky, A., V. K. Bhutani and I. Odame (2018). "Rhesus disease: a global prevention strategy." The Lancet Child & Adolescent Health 2(7): 536-542.