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Intrafetal laser for midtrimester TRAP sequence-experience from a single center

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Abstract

Objective: To report our experience and evaluate outcomes in monochorionic pregnancies with Twin Reversed Arterial Perfusion sequence with intrafetal laser therapy.

Methods: Retrospective review of records of all pregnancies with TRAP sequence treated by intrafetal laser therapy between 2011 January and 2015 December that were retrieved and analysed.

Results: Electronic search of the scan database retrieved 57 cases of TRAP sequence during the study period, 7 triplets and 50 monochorionic twins. Intrafetal laser was done in 27 cases, 22 cases of twins and 5 cases of triplets. In the twins group, median gestational age at intervention was 22.5 weeks, the earliest done at 16.3 weeks. The median gestational age at delivery and birth weight was 37 weeks and 2.5 Kgs. The median procedure and delivery interval was 14 weeks. Live birth rate was 17/22 (77%) the pump survival rate was 16/22 (73%). Pregnancies with non-surviving pump were 5 in numbers (5/22). A repeat procedure was warranted in one case. In the triplet group, median gestational age at intervention, delivery and procedure delivery interval was 18, 35 and 17 weeks.

Conclusion: Intrafetal laser is simple, effective and the treatment of choice to interrupt the vascular supply to acardiac twin.

1 | INTRODUCTION

Twin Reversed Arterial Perfusion (TRAP), also referred to as acardiac twinning, is a unique and rare complication of monochorionic pregnancies wherein the acardiac foetus is perfused by an apparently normal (pump) foetus (Figure 1). It is the most extreme form of inter-twin transfusion, occurring in approximately 1% of monochorionic pregnancies and 1 in 35 000 pregnancies overall.[1] It requires monochorionic placentation and a large artery to artery (AA) anastomosis between the two fetal circulations, through which deoxygenated blood is shunted from the umbilical artery of the pump twin into the umbilical artery and mainly the iliac vessels of the co-twin. The natural history is unknown, yet several authors have recommended interventions to arrest the flow to the perfused twin. Various techniques including ultrasound guided coil embolization, injection of absolute alcohol, bipolar cord coagulation, intrafetal laser, Radio Frequency Ablation (RFA), fetoscopic cord ligation and laser photocoagulation of the anastomoses have been reported with varying success rates.[2] Many of the series include a mix of indications and conditions, yet rarely deal uniquely with TRAP-sequence. Spontaneous death of the pump twin before intervention and spontaneous arrest of flow have been reported.[3] Authors have also compared the different methods of umbilical cord occlusion to determine the best method and look at reasons for fetal loss from RFA.[4,5] Herein we report a single center experience with this rare condition, including those managed expectantly as well as by ultrasound-guided intrafetal laser therapy in the second trimester using a standardized protocol. This information is relevant as there is a debate on whether TRAP sequence should be treated from the moment of diagnosis, or whether there is place for later treatment or expectant management.

Abbreviations: AA, artery to artery; DCTA, dichorionic triamniotic; IUFD, intra uterine fetal death; LSCS, lower segment caesarean section; MCDA, monochorionic diamniotic; MCMA, monochorionic monoamniotic; MCTA, monochorionic triamniotic; RFA, radiofrequency ablation; ROM, rupture of membranes; TRAP, twin reverse arterial perfusion.

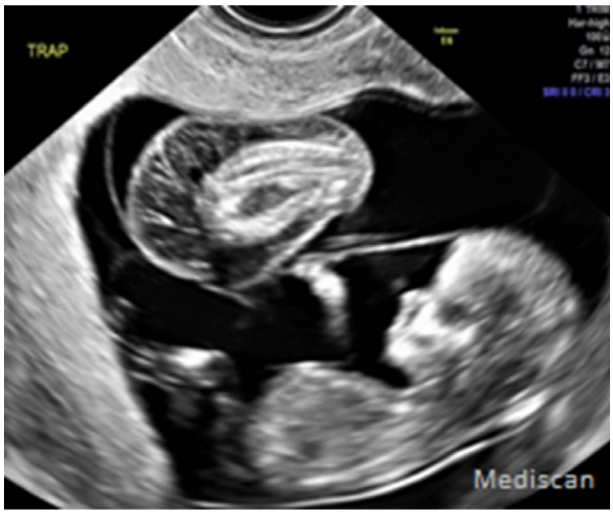

FIGURE 1 Trans vaginal first trimester image of perfused and pump foetuses

What is already known about this topic

Of the various interventions recommended for TRAP sequence ultrasound guided intrafetal laser therapy is an established technique.

What does this study add

Our study adds some evidence on the finer details related to the technique of intrafetal laser for TR.

2 | METHODS

This is a retrospective review of all monochorionic twins and triplets complicated by TRAP sequence managed in a 5-years period. 57 cases were retrieved from our fetal database (Sonocare Medialogic Solutions, Chennai, India). Those where intrafetal laser was performed were analysed separately. All underwent detailed sonographic evaluation by one of two senior operators for confirmation of retrograde perfusion from the normal twin to the acardiac fetus by color flow Doppler mapping. All pregnancies were followed up closely. Conservative management was offered if the gestational age was <16 weeks, the volume of the acardiac twin was <50% of that of the pump twin, when there was no or minimal vascularization on colour Doppler (PRF set at 0.6 kHz). These women were followed up on a fortnightly basis with Doppler study and 3D volume assessment of the perfused twin, until an adequate gestational age was reached to allow delivery. In all others, intervention was offered. Also in all triplets an invasive procedure was offered. Detailed counseling regarding the procedure and its complications was given and informed consent obtained. An institutional ethical committee (FCRF IEC) approval was obtained for this retrospective review.

Intrafetal laser was performed under ultrasound guidance and local anaesthesia, using an 18-gauge needle with a free-hand technique. A single dose of prophylactic antibiotic (cephalexin 1 g IV) was given before the procedure. A safe site of entry was identified to avoid a transplacental insertion or areas of high vascularity whenever possible. The umbilical vein and artery were identified at the hilus of the acardiac twin. The needle was advanced into the acardiac mass and positioned perpendicular to the vessels, with the tip at a distance of 1 cm from the vessels based on colour Doppler interrogation. A 600-nm laser fibre was passed through the needle, until the fiber tip was seen to indent the target vessel. It was then withdrawn by 2 mm and 30 W laser energy was delivered intermittently for 4 to 5 seconds using a diode-laser source (Your Lase 60, Transcot, Geneva Switzerland) until complete cessation of flow was confirmed by colour Doppler. Initial positioning and visualisation is important since with the first burst of laser energy, the area becomes echogenic compromising subsequent visualisation of the fiber tip. Patients were observed overnight and discharged and followed up with Doppler daily for 3 days, fortnightly for a month and monthly thereafter.

The main outcome measurements were technical failure, intrauterine death of the pump twin, intervention to delivery interval, rupture of the membranes, gestational age at delivery, birth weight and neonatal complications. The data was analysed separately for twin and triplet pregnancies.

3 | RESULTS

We traced 57 cases, that is, 50 monochorionic twins (diamniotic = 47, monoamniotic = 3) and 7 triplets (monochorionit triamniotic = 2, dichorioinic tri-amniotic = 5) in our database (Figure 2).

Among the 50 twins, there was an anomaly in the pump twin in six cases (MCDA = 4, MCMA = 2) and hydrops in one case. These 7 patients opted for termination of the pregnancy. The structural abnormalities included congenital heart defects (n = 2), idiopathic intra-arterial calcification, limb body wall complex, anencephaly, multisystem anomaly (pulmonary stenosis, short femur, single umbilical artery). In 11 cases, conservative management and follow up was advised. Intervention was advised in the remaining 32 cases (Table 1). Six of these opted for termination of pregnancy, four declined intervention and opted for expectant management. All these four had an adverse outcome (Intra Uterine Fetal Death = 2, mid-trimester pregnancy loss = 2, at 23 and 25 weeks respectively).

Therefore, 22 cases of twins consented for intervention (Table 2). The cervical length was normal in 20 cases and two cases had a short cervix (<2.5 cm). The median gestational age at intervention was 22.5 weeks (IQR −19.75, 24.00), the earliest intervention in twins was at 16.3 weeks. In two cases laser was done at 26 weeks, because of a late diagnosis.

There were five pregnancies with a non-surviving pump (5/22). Two were mid-trimester losses (rupture of membranes

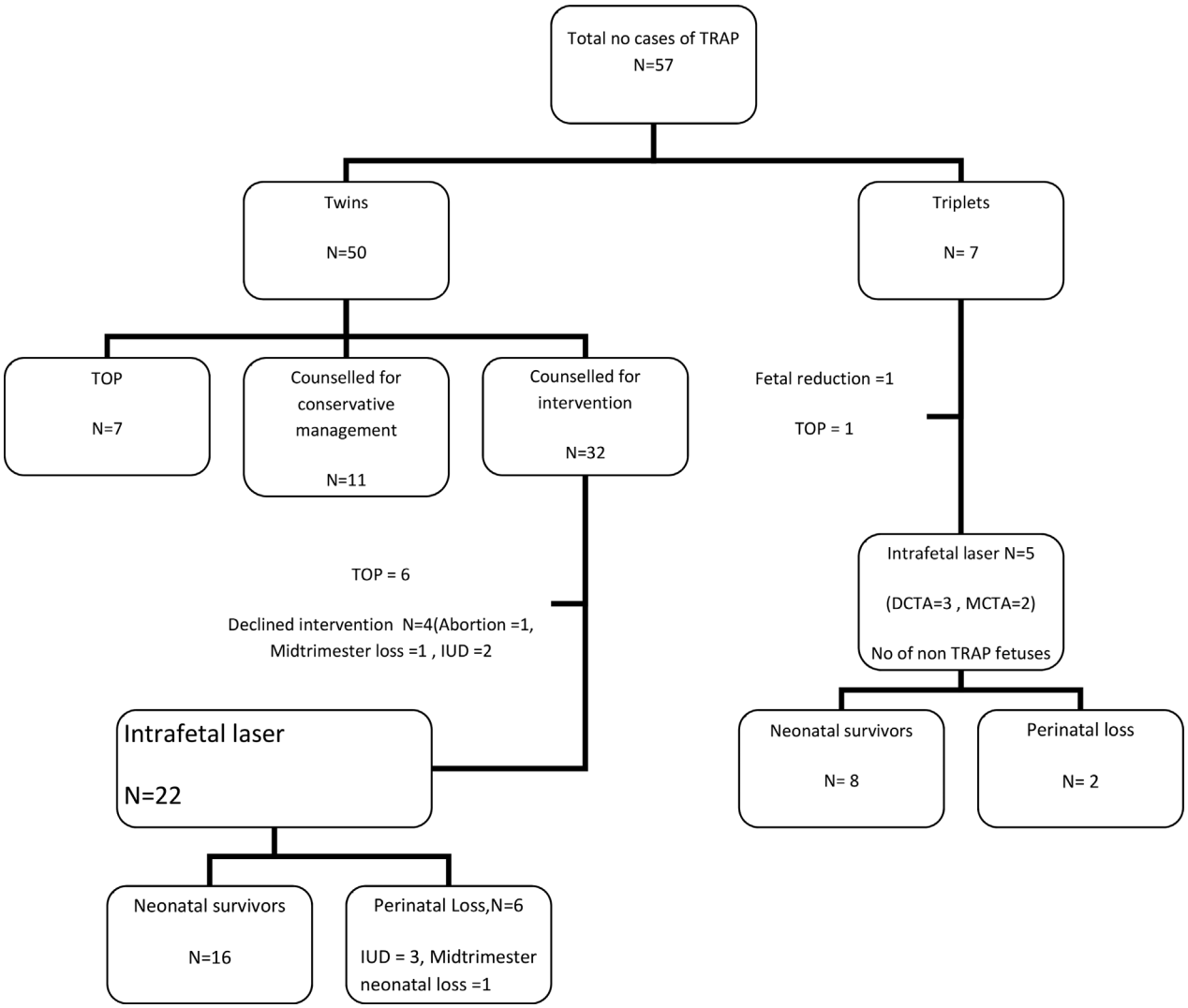

FIGURE 2 Flow chart of the cases with TRAP sequence with their outcomes. (TOP, termination of pregnancy; DCTA, dichorionic triamniotic; MCTA, monochorionic triamniotic)

[ROM] followed by expulsion). Gestational age at procedure in these cases were 22 and 25.1 weeks respectively, one of which had polyhydramnios. There were three intrauterine fetal deaths (IUFD) of the pump twin, two within 48 hours of the procedure. In both cases the two vessels were not parallel and diverging from each other at the hilum. Both fetuses showed a high MCA PSV when reviewed the next day. There was one late IUFD 10 weeks after the procedure. At follow up 4 weeks post procedure the perfused fetus significantly reduced in volume with no flow and the pump fetus was normal with normal Doppler findings. A repeat procedure was done in one case. On the third day post laser (18 weeks) minimal flow was noticed on color Doppler with low PRF (0.6 kHz) and during follow up the volume of the perfused fetus increased from 146 cc to 231 cc at 21 weeks, so that we decided to offer a repeat laser. The procedure delivery interval in this case was 19 weeks.

The median gestational age at delivery 37.0 weeks (IQR: 36.1, 38.0). The median procedure to delivery interval was 14 weeks (IQR: 9.5-15.5) (Figure 3). The median birth weight was 2500 g (IQR: 2137, 3050). Structural abnormalities noted in the pump twin were a ventricular septal defect (n = 2) and a single umbilical artery (n = 3) and talipes equinovarus (n = 1). The overall live birth rate of the pump twin was 17/22 (77%). Seven (33%) were born preterm (28-36 weeks). One baby born at 32 weeks developed respiratory distress syndrome and died in the NICU 1 week later. The procedure delivery interval in this case was 14 weeks. The neonatal survival rate therefore in our series was 16/22 (73%).

Among the twins with TRAP in whom we had proposed conservative management (n = 11), the median gestational age at diagnosis was 16.5 weeks (IQR:13.0-19.3), median gestational age at delivery 37.1 weeks (IQR: 34.2, 37.2) and birth weight was 2500 g (IQR:1850, 2900).The live birth rate was 90.9% (10/11). There was one in utero fetal death. This patient was first seen at 17.6 weeks, with a TRAP mass of 4.9 cc (pump twin mass 69 cc) yet without detectable flow on colour Doppler examination. On follow up 4 weeks later an IUFD was diagnosed.

TABLE 1 Split up details of the twin pregnancies that underwent intrafetal laser

#	G age at referral (weeks)	G age at pro (weeks)	Pro Delivery interval (weeks)	Structural abn/Growth abn in pump	Treatment failure	IUD/NND/ Midtrimester loss	ROM/ Preterm l/Expulsion	G age at delivery (weeks)	Outcome	Comment
1	22	22	2 days	-	+	+	-		Fetal loss	IUD –48 hours of procedure
2	24	24	3 days	-	+	+	+		Fetal loss	Expelled within 72 hours of procedure
3	26.3	26.3	13	SUA	-	-	-	39	Live born	
4	23	23	15	-	-	-	-	38	Live born	NICU <1 week
5	23	23	15	-	-	-	-	38	Live born	
6	17	18	19	-	-	-	-	37	Live born	Repeat procedure at 21 weeks
7	18	19	10	Bil CTEV	-	+	-	29	Fetal loss	IUD 10 weeks after procedure
8	21	25	11	-	-	-		36	Live born	
9	20	21	15	-	-	-	+	36	Live born	
10	16	16	21	-	-	-	-	37	Live born	
11	26	26	10	-	-	-	+	36	Live born	
12	16	18	14	-	-	+	+	32	Live born	LSCS, baby had respiratory distress-NND, 1 week after birth
13	24	24	8	-	-	-	+	32	Live born	NICU > 1 week
14	22	22	0	-	+	+		22	Fetal loss	Expelled within 24 hours of procedure
15	18	18	19	-	-	-	-	37	Live born	
16	24	24	14	-	-	-	-	38	Live born	
17	15	20	19	SUA			-	39	Live born	
18	25	25	2 days	SUA	+	+	+		Fetal loss	IUD –48 hours of procedure
19	23	23	14	VSD	-	-	_	37	Live born	Coexistant chorioangioma
20	12	21.1	14	VSD, IUGR	-	-	+	35	Live born	
21	24	24	15					39	Live born	
22	20	20	17	-	-	-	-	37	Live born	

Abbreviations: CTEV, congenital talipes equinus varus; G Age, gestational age; IUD, intra uterine demise; IUGR, intra uterine growth restriction; NICU, neonatl intensive care unit; NND, neonatal death; ROM, rupture of membranes; SUA, single umbilical artery; VSD, ventricular septal defect.

TABLE 2 The indications for intervention (N = 22 twins)

Indication for intervention	N	%
Features of compromise in pump	11	50
Increase in volume of trap/grossly hydropic trap	10	45
Coexistent Chorioangioma	1	5
Total	*22*	

In the group of triplet pregnancies (n = 7) (MCTA = 2, DCTA = 5), one patient declined intervention and one opted for fetal reduction of the MCDA pair with TRAP. The remaining 5 (MCTA = 2, DCTA = 3) underwent intrafetal laser(Table 3). The median gestational age at intervention, delivery and procedure delivery interval was 18, 35 and 17 weeks. Four delivered preterm, at 30, 33 and two at 35 completed weeks. One was delivered at 38 weeks. Two babies born at 30 and 33 weeks succumbed to respiratory distress and sepsis, all others are alive and healthy.

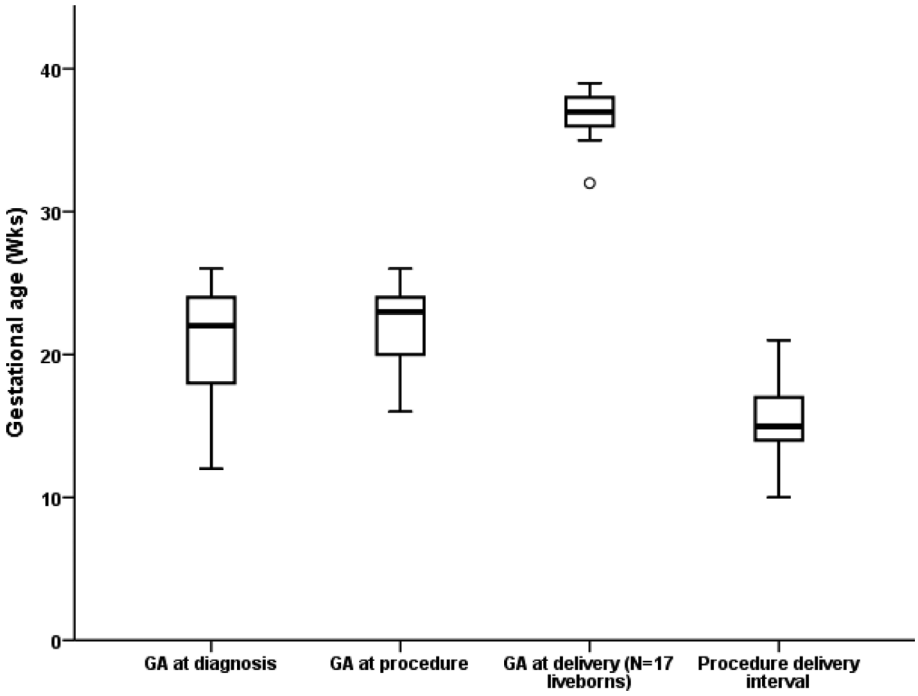

FIGURE 3 Gestational age at diagnosis (median 22 weeks, IQR-18, 24), at intervention (median 22.5 weeks, IQR-19.75, 24), at delivery (median 37 weeks. IQR −36.1, 38) of surviving twins, and the procedure delivery interval (median -14, IQR −9.5, 15.5). Boxes represent medians and interquartile ranges (IQR) and whiskers indicate ranges

TABLE 3 Details of triplet pregnancies intervened

#	Chorionicity	Ga at referral (weeks)	Indication for intervention	Ga at intervention (weeks)	Preterm/term delivery	Ga at delivery (weeks)	Birth weight (kg)	Perinatal outcome
1	DCTA	12	Feature of compromise–polyhydramnios	18	Preterm labour	35	Both 1.25	Both live
2	MCTA	17	Feature of compromise-Abnormal doppler	17	Term	38	2.3 & 2.5	Both live
3	DCTA	12	Increase in volume of trap	18	Preterm labour	35	Both 2	Both live
4	MCTA	20	Increase in volume of trap	23	Preterm labour	33	Both 1.2	NND & Live
5	DCTA	23	Feature of compromise-Abnormal doppler	23	Preterm labour	30	1.3 & 1 kg	NND & Live

Abbreviations: DCTA, dichorionic triamniotic; MCTA, monochorionic triamniotic; NND, neonatal death.

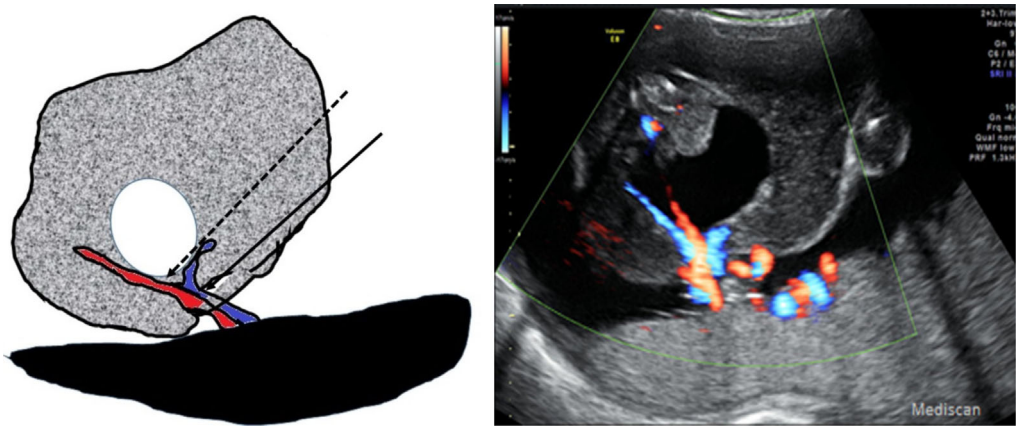

FIGURE 4 Left-Diagrammatic representation of vessel diverging after a very short course at the hilum. The arrow on dotted line points at the wrong site to coagulate. Right-B mode image with colour Doppler showing the vessels at the hilum

4 | DISCUSSION

Herein, we report on a consecutive series of 57 pregnancies complicated by TRAP sequence managed consistently. Intrafetal laser was performed in 27 cases (Twins –22, Triplets-5). In twins, the median gestational age at laser in cases with intact survival was 23 weeks, the pump twin live birth rate was 77% and neonatal survival rate was 73%. There was one repeat procedure done. IUFD of the pump twin occurred in 3 cases (13.6%). In two of three we think this was because the two target vessels entering the TRAP were not close to each other and diverging immediately after entry, as illustrated in Figure 4. Therefore, it is possible that the vessels were not both occluded simultaneously and exsanguination occurred. The hypothesis of exsanguination is supported by the observation of a high middle cerebral artery peak systolic velocity post procedure. Exsanguination into the placenta may theoretically also occur with complete occlusion, as through aberrant vessels the entire placenta can be perfused by a single twin, as recently described.[6] Identifying the apt site of occlusion especially in hydropic perfused twin may technically be challenging but a critical step in achieving success. In five triplet pregnancies undergoing laser, the median gestational age at delivery was 35 weeks. All the babies were born alive yet two succumbed in the neonatal period.

In 11 twin cases, conservative management was proposed based on predefined criteria described above. In this group there was a 90.9% live birth rate and one IUFD. The mean gestational age at delivery was 37 weeks.

Chaveeva et al[7] in a series of 104 cases of intrafetal laser, reported survival rates of 78.6% and 77.4% between 16-19 and 20-27 weeks, resp. at intervention. In our series, due to late referral, our timing of intervention was later (median 22.5 weeks) with a 77% live birth rate of the pump twin. When comparing with the cohort study and meta-analysis by Pagani et al,[8] the gestational age at intervention (median: 18.4 weeks) was later in our series. Intact neonatal survival rate was about 80%, and only 7% deliveries were prior to 32 weeks. The repeat procedure rate was 18% (n = 3) because of incomplete occlusion of blood flow or re-occurrence of flow in the TRAP mass. IUFD of the pump twin occurred in three cases (18%) at 5, 7 and 62 days after the procedure. In that study there were no neonatal deaths, while we had one neonatal loss among twins, because of respiratory distress. Post procedure, in our series, women went back to their respective towns for delivery. There may well be a variation in the level of neonatal care available at the different places of delivery in India and respiratory distress of prematurity and neonatal sepsis are still leading causes of neonatal mortality.[9,10] The outcomes in triplets are comparable to those described by Sepulveda et al,[11] Cavoretto et al,[12] and Smet et al[13] in Table 4.

This study obviously has many limitations. First it is describing a single center experience with its inherent bias towards patient selection and management preferences. Also it describes only a single technique, whereas other techniques are described with comparable outcomes. The setting was that of a country where the diagnosis of TRAP may be made later than in other countries where ultrasound detection of multiple gestation and its complications may be much earlier. However it describes how invasive fetal interventions can be safely and effectively transferred to countries where fetal therapy is still under development and not widely accessible. Also it describes the use of laser for this condition. As laser is available in centers also

TABLE 4 Outcome of triplet pregnancies with TRAP treated by intrafetal laser-pooled data

Author	GA at Diagnosis (Weeks)	Indication for intervention	Type of intervention	GA at Intervention (Weeks)	GA at Delivery (Weeks)	Outcome
Cavoretto et al 2009 (N = 1)	11	Increase in volume of trap	Intrafetal laser	19	35	Both A & H
Sepulveda et al 2009 (N = 2)	7	Increase in volume of trap	Intrafetal laser	17	34	Both A & H
	16	Features of compromise in pump-IUGR	Intrafetal laser	17	37	1-A & H, 1-Still born
Smet et al 2012 (N = 1, Double TRAP)	11	Increase in volume of trap	Intrafetal laser and transection of cord for both	15.6	32	One A & H
Current study.2016 (N = 5)	23	Features of compromise in pump	Intrafetal laser	23	30	1-A&H, 1-NND
	17	Features of compromise in pump	Intrafetal laser	17	38	Both A & H
	12	Increase in volume of trap	Intrafetal laser	18	35	Both A & H
	20	Increase in volume of trap	Intrafetal laser	23	33	1-A&H, 1-NND
	12	Features of compromise in pump	Intrafetal laser	18	35	Both A & H

Abbreviations: A & H, alive and healthy; NND, neonatal death.

offering chorionic plate vessel coagulation for transfusion syndrome, this is over there an instantly available option than for instance radiofrequency or microwave ablation. Lastly, this cohort study also includes a number of expectantly managed cases, demonstrating again that the outcome of selected cases of TRAP may be good. Because of the rarity of the condition, such detailed data may be useful.

5 | CONCLUSION/SUMMARY

Intrafetal laser is a simple, effective technique, and we use it as the technique of choice to interrupt the vascular supply to an acardiac twin. Conservative management is a potential option in a very select group of TRAP sequence cases. Though in our series, interventions were done later in gestation, the live birth rate (77%) and neonatal survival rate (73%) was comparable to what as reported. This experience demonstrates that the technique can be implemented in countries where advanced invasive therapeutic techniques are new, and where the diagnosis of TRAP may be made at a later stage in gestation. Failures may be due to technical reasons.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

ETHICAL APPROVAL STATEMENT

Ethical committee approval obtained (Study No - FCRF/EC/2015/003).

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REFERENCES

1. Wong AE, Sepulveda W. Acardiac anomaly: current issues in prenatal assessment and treatment. *Prenat Diagn*. 2005;25:796-806.
2. Tan TY, Sepulveda W. Acardiac twin: a systematic review of minimally invasive treatment modalities. *Ultrasound Obstet Gynecol*. 2003;22:409-419.
3. Lewi L, Valencia C, Gozalez E, et al. The outcome of twin reversed arterial perfusion sequence diagnosed in the I trimester. *Am J Obstet Gynecol*. 2010;203:213.e1–4.
4. Abdel-Sattar M, Chon AH, Llanes A, Korst LM, Ouzounian JG, Chmait RH. Comparison of umbilical cord occlusion methods: radiofrequency ablation versus laser photocoagulation. *Prenat Diagn*. 2018;38(2):110-116.
5. Sun L, Zou G, Yang Y, Zhou F, Tao D. Risk factors for fetal death after radiofrequency ablation for complicated monochorionic twin pregnancies. *Prenat Diagn*. 2018;38(7):499-503.
6. Deneckere S, Couck I, Devlieger R, et al. Placental vascular recruitment after single intrauterine demise: a newly diagnosed phenomenon unique to monochorionic pregnancies. *Prenat Diagn*. 2019;39:409-412.
7. Chaveeva P, Poon LC, Sotiriadis A, Kosinski P, Nicolaides KH. Optimal method and timing of intrauterine intervention in twin reversed arterial perfusion sequence: case study and meta-analysis. *Fetal Diagn Ther*. 2014;35:267-279.
8. Pagani G, D'Antonio F, Khalil A, Papageorghiou A, Bhide A, Thilaganatha B. Intrafetal laser treatment for twin reversed arterial perfusion sequence: cohort study and meta-analysis. *Ultrasound Obstet Gynecol*. 2013;42:6-14.
9. Verma J, Anand S, Kapoor N, Gedam S, Patel U. Neonatal outcome in new-borns admitted in NICU of tertiary care hospital in Central India: a 5-year study. *Int J Contemp Pediatr*. 2018;5(4):1364-1367.
10. Murthy S, Godinho MA, Guddattu V, Lewis LES, Nair NS. Risk factors of neonatal sepsis in India: a systematic review and meta-analysis. *PLoS One*. 2019;14(4):e0215683. https://doi.org/10.1371/journal.pone.0215683.
11. Sepulveda W, Wong AE, Bustos JC, Flores X, Alcalde JL. Acardiacfoetus complicating a triplet pregnancy: management and outcome. *Prenatal Diagn*. 2009;29:794-799.
12. Cavoretto C, Serafini A, Valsecchi L, Lanna M, Rustico MA. Early diagnosis, follow-up and prenatal treatment of a case of TRAP sequence occurring in a dichorionic triamniotic triplet pregnancy. *J Clin Ultrasound*. 2009;37:350-353.
13. Smet M-E, Smet D, DeKoninck P, De Catte L, Deprest J, Devlieger R. Prenatal surgery in a triplet pregnancy complicated by a double twin reversed arterial perfusion (TRAP) sequence. *Case Rep Perinat Med*. 2012;1(1-2):83-86.

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