Placenta and Reproductive Medicine

MINI REVIEW

YOUNG INVESTIGATOR CORNER

Twin reversed arterial perfusion sequence: A review of cases in the Philippines from 2000 to 2022

Ourlad Alzeus G. Tantengco[1,2], Clarissa L. Velayo[1,3]

[1]Cell and Developmental Physiology Laboratory, Department of Physiology, College of Medicine, University of the Philippines Manila, Manila 1000, Philippines;
[2]Department of Biology, College of Science, De La Salle University, Manila 0922, Philippines;
[3]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of the Philippines-Philippine General Hospital, Manila 1000, Philippines

Abstract

Twin reversed arterial perfusion (TRAP) sequence, or acardiac twinning, is a congenital anomaly associated with monochorionic twin pregnancies. It occurs when the cardiac system of one twin supplies blood for both twins. This congenital anomaly has been previously reported in several case reports from the Philippines. However, there is still limited information about its local epidemiology and management. This study reviewed the previous cases of TRAP sequence and discussed the diagnosis, management, and ways to improve care for pregnant patients affected by this condition. There were five reported cases of TRAP sequence from the Philippines. Ultrasonography was used in diagnosing the disease antenatally. Preterm birth was reported in 60% of the cases, while 80% were delivered *via* Cesarean section. The most common type of acardiac twinning in the Philippines was the acardius acephalus. The most common placentation observed in TRAP sequence cases was monochorionic, monoamnionic placenta (75%), two of which had arterio-arterial and veno-venous anastomoses. All donor twins in the Philippines were delivered alive, with only one (20%) neonatal death due to *Pseudomonas* infection. Only a few centers can perform minimally invasive fetal interventions; one center has been performing fetoscopic surgery in the Philippines since 2021. Thus, cases of TRAP sequence in the Philippines have only been managed through antenatal surveillance with serial ultrasound and high-risk prenatal care until their eventual delivery.

Key words: acardiac twinning, chorangiophagus parasiticus, congenital anomaly, multifetal pregnancy, twin reversed arterial perfusion sequence

INTRODUCTION

Twin reversed arterial perfusion (TRAP) sequence, or acardiac malformation, is a rare congenital anomaly associated with monochorionic multifetal pregnancies.[1,2] One of the twins lacks a complete cardiac structure (acardiac twin), while the other is morphologically normal and supports the circulation of the acardiac twin aside from supplying its own (pump twin).[1] The current incidence is 2.6% in monochorionic twin pregnancies and 1:9500 to 11,000 in all pregnancies.[3] The pathogenesis of TRAP sequence is not yet fully understood. However, it was proposed that the disease could be due to underlying vascular anastomoses in the monochorionic placenta. The twin with higher blood perfusion usually develops and becomes the pump twin, while the twin with decreased blood perfusion becomes the acardiac twin due to compromised morphogenesis.[1,4] Another hypothesis is that primary failure of heart development in one twin, due to a chromosomal abnormality or environmental

Peer review under responsibility of the Editorial Board.
Corresponding Author:
Dr. Ourlad Alzeus G. Tantengco, E-mail: ogtantengco@up.edu.ph; https://orcid.org/0000-0002-4535-8837

Citation:
Tantengco OAG, Velayo CL. Twin reversed arterial perfusion sequence: A review of cases in the Philippines from 2000 to 2022. *Placenta Reprod Med*. 2023;2:7.

DOI: 10.54844/prm.2023.0365

Received: 12 March 2023
Accepted: 25 April 2023
Published: 30 May 2023

This article was submitted to Young Investigator Corner, a section of the journal *Placenta and Reproductive Medicine* (PRM).

factors, ultimately leads to its perfusion by the pump twin through artery-artery anastomoses. A retrograde blood flow pattern through the umbilical arteries supports the unique perfusion of an acardiac fetus.[1,4] The acardiac twin is often mistaken to be viable, leading to conservative management or the reluctance to interrupt its blood supply through minimally invasive surgery. While this anomalous intertwin blood supply persists, the pump twin becomes increasingly at risk of developing congestive heart failure and polyhydramnios which may give rise to the complications of preterm delivery. This results in up to 55% perinatal mortality for the pump twin.

TRAP sequence has been previously reported in the Philippines.[5–9] However, there is still limited information regarding the local epidemiology and management of this disease. This study reviewed the previous cases of TRAP sequence in the country and discussed the diagnosis, management, and ways to improve care for pregnant patients affected by this condition. An extensive literature search in the Health Research and Development Information Network (HERDIN) database, the national health research repository of the Philippines, was conducted using the keywords: twin reversed arterial perfusion sequence, TRAP sequence, acardiac twin, acephalus twin, and chorangiophagus parasiticus. Relevant original articles and case reports in English and Filipino were included in this review.

TRAP SEQUENCE IN THE PHILIPPINES

The first case of monoamnionic twinning in the Philippines was reported in 1946.[10] In our hospital, the Philippine General Hospital, there were 1752 delivered babies with multiple congenital anomalies from 2010 To 2022. Of these, only three were recorded as cases of acardiac twinning (0.17%). During the 21st century, we obtained five distinct cases of TRAP sequence from the Philippines (Table 1).[5–7,9] Three additional cases were reported but with notably incomplete clinical data. Hence, they were not included in this review.

The maternal age range of TRAP sequence patients in the Philippines was 27 to 41. The most common maternal comorbidity was preeclampsia (2 out of 5). The diagnosis of TRAP sequence was made *via* ultrasonography. Three TRAP sequence patients were delivered preterm (60%) and two at term (40%). Most were delivered *via* Cesarean section (80%), and only one was *via* vaginal delivery (20%). The most common type of acardiac twinning in the Philippines is the acardius acephalus type, where the fetus has a well-developed pelvis and lower limbs but no head, usually no thoracic organs, and no upper limbs. This is also the most common type worldwide.[11] The birth weight range of the donor or pump twin was 1250 g to 2500 g, while the acardiac twin ranged from 500 g to 1950 g. Only four cases reported the amnionicity and chorionicity of the placentas. The most common were monochorionic, monoamnionic placentae (75%), where two patients had arterio-arterial and veno-venous anastomoses. Only one patient had monochoronic, diamnionic placenta (25%). Lastly, all donor twins in the Philippines were delivered alive, with only one (20%) neonatal death due to *Pseudomonas* infection. This fetus was delivered alive with hydrops fetalis, cardiomegaly, and hepatomegaly.

DIAGNOSIS OF TRAP SEQUENCE IN THE PHILIPPINES

The prenatal diagnosis of acardiac twinning or TRAP sequence in the Philippines is commonly *via* ultrasonography alone. TRAP sequence can be diagnosed at the end of the first trimester, where one of the twins is found to be a hydropic fetus without cardiac activity.[12,13] The acardiac twin may also present with several head, trunk, or limb malformations, as well as with subcutaneous edema or with other areas of excess fluid accumulation. Intertwin growth discrepancies in the biometrical measurements of the twins, particularly in the abdominal circumference, are also typical findings in TRAP sequence patients.[11,14] Furthermore, a pathognomonic feature of reverse flow within arterio-arterial anastomoses in the umbilical arteries can be seen in Doppler studies. This is characterized by a paradoxical circulation where arterial blood flows towards the acardiac twin in a caudal to cranial pattern through the abdominal aorta.[1,15]

It is important to establish the correct diagnosis for TRAP sequence patients. Misdiagnosis may lead to adverse outcomes for the pump twins. Differential diagnoses for TRAP sequence that should be ruled out include chorioangioma, a placental cyst or teratoma, and an early single demise in a monochorionic twin pregnancy.[16]

MANAGEMENT OF TRAP SEQUENCE IN THE PHILIPPINES

The acardiac twin is 100% not viable.[17] Hence, the management of TRAP sequence should prioritize the prevention of complications in the pump fetus and the mother and maintain the pregnancy for delivery at term. Based on the current evidence and consensus of experts, minimally invasive techniques are associated with the best prognosis with minimal maternal and fetal risks. Available interventions include ultrasound-guided and fetoscopic-guided treatments.[11] Ultrasound-guided and fetoscopic-guided treatments can directly target the umbilical cord vessels of the acardiac twin. Ultrasound-guided umbilical cord occlusion techniques involve using thrombogenic steel coils, alcohol-soaked suture material, glucose, fibrin, enbucrilate gel, ligation, or electrical energy in the form of monopolar or bipolar thermocoagulation.[11,18,19] These interventions are usually carried out at or after 16 weeks of gestation. However, several studies reported that

Table 1. Summary of cases of twin reversed arterial perfusion sequence in the Philippines

Maternal age and obstetric score	Maternal comorbidities	Diagnosis of twins in gestational week	Malformation of the donor twin	Gestational age at delivery	Mode of delivery	Birth weight	Amnionicity and chorionicity of the placenta	Outcome for donor twin	Ref
27 years old, G2P1 (1001)	None	Not reported	Acardiac, with multiple congenital anomalies (not specified)	32 4/7 weeks	Primary low segment Cesarean section	Donor: 1600 g Acardiac: 500 g	Not reported	Live birth, with hydrops fetalis, cardiomegaly and hepatomegaly, but later died due to sepsis secondary to *Pseudomonas* infection	[6]
34 years old, G2P1 (0101)	Uncontrolled preeclampsia	22 weeks	Acardiac, acephalus, bilateral equinovarus deformity, underdeveloped testes, and empty thoracic cavity	30 weeks	Cesarean section	Donor: 1250 g Acardiac: 1950 g	Monochorionic, diamnionic with a single umbilical artery	Live birth, with inguinal hernia	[9]
41 years old, G8P7 (7007)	Diffuse toxic goiter in impending storm; Chronic hypertension with superimposed preeclampsia; Anemia	23 1/7 weeks	Acardiac, acephalus, absent esophagus, liver, pancreas and gallbladder, Meckel's diverticulum, imperforate anus with persistent cloaca, omphalocele, undescended testis, fused kidneys, oligodactyly in the left foot, and pedal hypoplasia in the right foot	32 6/7 weeks	Donor: Spontaneous vaginal delivery Acardiac: Partial breech extraction	Donor: 1300 g Acardiac: 1800 g	Monochorionic, monoamnionic, weighing 600 g, with several superficial arterio-arterial and veno-venous anastomoses	Live birth, morphologically normal except for cardiomegaly with left ventricular hypertrophy	[5]
37 years old, G3P2 (2002)	None	32 weeks	Acardius anceps amorphous type, omphalocele, imperforate anus, absent external genitalia, deformed cranial vault, undeveloped diaphragm, ascites, anasarca, and a single lower extremity with oligodactyly	37 weeks	Repeat low segment Cesarean section	Donor: 2500 g Acardiac: 1250 g	Monochorionic, monoamnionic placenta with artery to artery and vein to vein anastomoses	Live birth, morphologically normal	[5]
35 years old, G1P0	None	23 2/7 weeks	Acardiac amorphous component	38 to 39 weeks	Cesarean section	Donor: 2490 g Acardiac: 1500 g	Monochorionic, monoamnionic placenta with a three-vessel cord	Live birth, conjoined twinning, pyopagus type, no sharing of major organs and vessels with the conjoined twin	[7]

ultrasound-guided bipolar thermocoagulation resulted in higher rates of miscarriage when performed at 16–19 weeks compared to those treated after 19 weeks.[20,21] On the other hand, fetoscopic-guided treatment may involve ligating the umbilical cord or coagulating the umbilical vessels using laser energy.[22] A previous study showed that fetoscopic-guided umbilical cord occlusion achieved better pregnancy outcomes if performed at or before 24 weeks of gestation.[11,23] Endoscopic laser coagulation at 26 and 28 weeks of gestation failed to arrest blood flow because the umbilical cords were very edematous.[23]

The main disadvantage of the cord occlusion techniques is the technical difficulty of correctly targeting the umbilical vessels of the acardiac twin,[11] which usually lie close to that of the pump twin. Consequently, this procedure can also damage the cord of the pump twin. Moreover, the umbilical cord of the acardiac twin is short, thin, and highly susceptible to rupturing and bleeding. To avoid these complications, ultrasound-guided intrafetal techniques were developed. Intraabdominal vessels can be easily visualized with color Doppler ultrasound allowing proper targeting of an acardiac twin's abdominal aorta or pelvic

vessels. Intrafetal ablation techniques include alcohol chemosclerosis, monopolar diathermy, laser coagulation, and radiofrequency ablation.[24–26] These techniques are performed between 16 weeks age of gestation to as long as 30 weeks age of gestation, although some centers have reported that elective treatment with intrafetal laser therapy between 13 and 16 weeks' gestation decreased adverse outcomes for pregnancies with TRAP sequence.[27] Another study showed that prophylactic intervention by intrafetal laser from 12 weeks onward was associated with lower rates of preterm birth and preterm premature rupture of membranes. It was also associated with higher gestational age and birthweight than the expectant approach until 19 weeks' gestation with subsequent radiofrequency ablation.[28]

Until this article was written, there have been no known reported attempts of minimally invasive treatment to address cases of TRAP sequence in the Philippines. As of 2022, there were 247 licensed Maternal Fetal Medicine (MFM) specialists in the country, most of whom maintained their practices in highly urbanized or metropolitan areas.[29] Currently, only a few centers can perform minimally invasive fetal interventions, and only one center has been performing fetoscopic surgery since 2021. Thus, cases of TRAP sequence in the Philippines have only been managed through antenatal surveillance with serial ultrasound coupled with high-risk prenatal care until their eventual delivery.

CONCLUSIONS AND PERSPECTIVES

This review listed the five reported cases of TRAP sequence in the Philippines during the 21st century. The low sample size of cases of TRAP sequence is a major limitation of this review. However, based on the available information, we discussed the diagnosis and available management of this disease in the Philippines. Ultrasonography remains the standard method in diagnosing TRAP sequence in the country, while minimally invasive umbilical cord and intrafetal vessel occlusion techniques have yet to be attempted. There is still a significant need for research and development in the clinical management of TRAP sequence and most other fetal interventions locally.

One of the gaps in clinical practice is the low number of MFM specialists trained in diagnosing and caring for patients with TRAP sequence in the Philippines. Most of these specialists are concentrated only in major cities. Looking at the bigger picture, this maldistribution of specialists has contributed to socioeconomic and geographical disparities in available antenatal care and birth outcomes.[30,31] For instance, only 68.5% of women residing in the Autonomous Region of Muslim Mindanao have been reported to receive antenatal care during pregnancy. This contrasts with 98% of antenatal care coverage among women in the Eastern Visayan Region. Moreover, there are still regions in the Philippines where many pregnant women deliver outside a health facility.[30] Therefore, many cases of TRAP sequence and other complications of multiple gestations may fail to be diagnosed and result in poor maternal and neonatal outcomes.

There is also insufficient research on TRAP sequence and other complications of multifetal pregnancy in the Philippines. Moreover, there is limited epidemiologic data on TRAP sequence due to several reasons: (1) low funding opportunities and priority allocation for antenatal health research on rare conditions; (2) lack of a national registry of multiple congenital anomalies with emphasis on prenatal diagnosis; and (3) few physicians publishing cases of TRAP sequence. There is a need for more studies on TRAP sequence and other complications of multifetal pregnancies to determine the actual burden of the disease in the Philippines. We encourage Filipino physicians to publish their cases of TRAP sequence, and for Obstetrics and Gynecology or MFM specialty societies to develop a national registry of multiple congenital anomalies incorporating both prenatal and postnatal data. This registry can help gather epidemiologic data from all regions of the Philippines and be utilized as supporting evidence to prioritize research funding for the study of perinatal conditions to improve overall clinical management strategies in the population.

DECLARATIONS

Author contributions

Tantengco OAG: Conceptualization, Methodology, Investigation, Writing—Original draft preparation. Velayo CL: Conceptualization, Writing—Reviewing and Editing.

Conflict of interests

None declared.

REFERENCES

1. Vitucci A, Fichera A, Fratelli N, Sartori E, Prefumo F. Twin reversed arterial perfusion sequence: current treatment options. *Int J Women's Health.* 2020;12:435–443.
2. Benirschke K. The monozygotic twinning process, the twin-twin transfusion syndrome and acardiac twins. *Placenta.* 2009;30(11):923–928.
3. van Gemert MJC, van den Wijngaard JPHM, Vandenbussche FPHA. Twin reversed arterial perfusion sequence is more common than generally accepted. *Birth Defects Res A Clin Mol Teratol.* 2015;103(7):641–643.
4. Søgaard K, Skibsted L, Brocks V. Acardiac twins: pathophysiology, diagnosis, outcome and treatment. Six cases and review of the literature. *Fetal Diagn Ther.* 1999;14(1):53–59.
5. Silao JNI. Twin Reversed – Arterial Perfusion Sequence : The Experience of a Tertiary Referral Hospital in the Philippines with Acardiac Twinning. *Acta Med Philipp.* 2009;43:61–69.
6. Ramos-Costa CJS, Tansengco LG. "When Heartbeats Are Shared ..." A Case of Acardiac Twinning. *Philipp J Obs.* 2004;28:81–85.
7. Ipac-Alavazo ARP, Go-Du J, Jesalva-Martinez KA. A Rare Case of Term Triplet Pregnancy Complicated with Twin Reversed Arterial Perfusion : Conjoined Pump and Acardiac Acephalus Twins with an Acardiac Amorphous Triplet *. *Philipp J Obstet Gynecol.* 2012;36:84–92.

8. Mamaril SDL. Twins: Acardiac Acephalus and Hydrops Fetalis. *Philipp Sci J*. 2005;38(2):65–69.
9. Pascual CG, Tan FL, Pichar RL. An Angel in Disguise : Twin Reversed Arterial Perfusion. *Philipp J Obstet Gynecol*. 2006;30(4):211–218.
10. ACOSTA-SISON H, ARAGON GT, De La PAZ A. Mono-amniotic twins; danger to the life of at least one twin. *J Philipp Med Assoc*. 1946;22(2):43–46.
11. Wong AE, Sepulveda W. Acardiac anomaly: current issues in prenatal assessment and treatment. *Prenat Diagn*. 2005;25(9):796–806.
12. Abouie A, Rakhshankhah N, Younesi L, Safarpour Z, Roostaee A, Amjad G. Twin reversed arterial perfusion sequence in a monochorionic monoamniotic twin pregnancy: a very rare condition. *Egypt J Radiol Nucl Med*. 2020;51(1):233.
13. Langlotz H, Sauerbrei E, Murray S. Transvaginal Doppler sonographic diagnosis of an acardiac twin at 12 weeks gestation. *J Ultrasound Med*. 1991;10(3):175–179.
14. Sepúlveda WH, Quiroz VH, Giuliano A, Henríquez R. Prenatal ultrasonographic diagnosis of acardiac twin. *J Perinat Med*. 1993;21(3):241–246.
15. Buyukkaya A, Tekbas G, Buyukkaya R. Twin reversed arterial perfusion (TRAP) sequence; characteristic gray-scale and Doppler ultrasonography findings. *Iran J Radiol*. 2015;12(3):e14979.
16. Lewi L, Couck I. Twin Reversed Arterial Perfusion Sequence: Pathophysiology and In Utero Treatment. In: Johnson A, Oepkes D, Kilby MD, eds. *Fetal Therapy: Scientific Basis and Critical Appraisal of Clinical Benefits*. Cambridge University Press; 2020: 398–403.
17. van Allen MI, Smith DW, Shepard TH. Twin reversed arterial perfusion (TRAP) sequence: a study of 14 twin pregnancies with acardius. *Semin Perinatol*. 1983;7(4):285–293.
18. Holmes A, Jauniaux E, Rodeck C. Monopolar thermocoagulation in acardiac twinning. *BJOG*. 2001;108(9):1000–1002.
19. Nicolini U, Poblete A, Boschetto C, Bonati F, Roberts A. Complicated monochorionic twin pregnancies: experience with bipolar cord coagulation. *Am J Obstet Gynecol*. 2001;185(3):703–707.
20. 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(4):267–279.
21. Lanna MM, Rustico MA, Dell'Avanzo M, *et al*. Bipolar cord coagulation for selective feticide in complicated monochorionic twin pregnancies: 118 consecutive cases at a single center. *Ultrasound Obstet Gynecol*. 2012;39(4):407–413.
22. Tan TT, Sepulveda W. Acardiac twin: a systematic review of minimally invasive treatment modalities. *Ultrasound Obstet Gynecol*. 2003;22(4):409–419.
23. Ville Y, Hyett JA, Vandenbussche FA, Nicolaides KH. Endoscopic laser coagulation of umbilical cord vessels in twin reversed arterial perfusion sequence. *Ultrasound Obstet Gynecol*. 1994;4(5):396–398.
24. Tsao K, Feldstein VA, Albanese CT, *et al*. Selective reduction of acardiac twin by radiofrequency ablation. *Am J Obstet Gynecol*. 2002;187(3):635–640.
25. Chao AS, Hsieh CC, Liou JD, Soong YK. Application of monopolar thermocoagulation in an acardiac fetus. *Prenat Diagn*. 2002;22(6):499–500.
26. Sepulveda W, Sebire NJ. Acardiac twin: too many invasive treatment options—the problem and not the solution. *Ultrasound Obstet Gynecol*. 2004;24(4):387–389.
27. Pagani G, D'Antonio F, Khalil A, Papageorghiou A, Bhide A, Thilaganathan B. Intrafetal laser treatment for twin reversed arterial perfusion sequence: cohort study and meta-analysis. *Ultrasound Obstet Gynecol*. 2013;42(1):6–14.
28. Berg C, Holst D, Mallmann MR, Gottschalk I, Gembruch U, Geipel A. Early vs late intervention in twin reversed arterial perfusion sequence. *Ultrasound Obstet Gynecol*. 2014;43(1):60–64.
29. Rivera FB, Magalong JV, Tantengco OA, Mangubat GF, Villafuerte MG, Volgman AS. Maternal and neonatal outcomes among pregnant women with cardiovascular disease in the Philippines: a retrospective cross-sectional study from 2015-2019. *J Matern Fetal Neonatal Med*. 2022;35(25):9922–9933.
30. Tantengco OAG, Ornos EDB. Trends in health insurance and antenatal care coverage in the Philippines. *J Public Health (Oxf)*. 2023;45(1):e146–e147.
31. Lintao RCV, Llamas-Clark EF, Tantengco OAG. Socioeconomic disparities in adverse birth outcomes in the Philippines. *Lancet Reg Health West Pac*. 2022;21:100453.