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REVIEW ARTICLE

# Diagnosis and Management of Fetal Ductus Arteriosus Constriction

**Bindiya D. Chugh**[1] · **Adinarayana Makam**[1]

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**Abstract** The ductus arteriosus is an important structure in the fetal circulation. It connects the pulmonary artery to the arch of the aorta distal to the origin of the left subclavian artery and carries most of the right ventricular output. Patency of the ductus arteriosus is maintained by factors like prostaglandin E2, nitric oxide and low oxygen tension of the blood. With the advent of ultrasonography and Spectral Doppler, many cases of ductal constriction have been reported. It can be idiopathic but is usually secondary to the use of medication like NSAIDs, isoxsuprine, fluoxetine and also some particular foods rich in polyphenol like herbal teas, dark chocolate, berries and coffee. Idiopathic ductal constriction is a rare finding. Ductus arteriosus constriction occurs largely due to inhibition of the prostaglandin synthetase pathway as the ductus arteriosus becomes more sensitive to prostaglandin inhibitors in later gestation. It is, therefore, more commonly seen in the 3rd trimester. Because of fetal hyperdynamic compromise, it results in tricuspid regurgitation, right ventricular hypertrophy and ultimately right ventricular failure, hydrops, pulmonary hypertension and even intrauterine fetal death. We present a series of ductus arteriosus constriction, of which 3 cases were associated with tricuspid regurgitation, 1 case with right sided dominance of the heart and 1 case with moderate to severe right ventricular hypertrophy. Mild cases require close fetal monitoring and severe cases may need urgent delivery. Postnatal prognosis seems to be good in cases of ductal constriction associated with right heart abnormalities as right heart abnormalities resolve in a couple of weeks, although pulmonary hypertension and right ventricular failure are major concerns. Preventive measures include avoiding the use of NSAIDs and other medications especially in the 3rd trimester and changes in maternal dietary habits.

**Keywords** Ductus arteriosus constriction · Ductal constriction · Spectral doppler · NSAIDs · Polyphenol rich foods · Right ventricular failure

## Introduction

The ductus arteriosus (DA) is an essential structure in fetal circulation. It connects the pulmonary artery to the aortic arch during fetal life. It starts to close within the first few hours after birth and gets obliterated by 72 hours of age to establish an adult circulation pattern. Patency of the ductus arteriosus is maintained by various factors such as prostaglandin E2, nitric oxide (NO) and low oxygen tension of the blood [1].

Since the introduction of spectral Doppler and fetal echocardiography, many cases of ductal constriction have been reported. Prior to the use of ultrasound, this was a diagnosis made only at autopsy of the severely hydropic fetus [2].

Premature ductal constriction is defined as a significant narrowing of the patent ductus arteriosus (PDA) during pregnancy. It is common in the third trimester as the DA becomes more sensitive to Prostaglandin synthetase inhibitors during this period. It results because of inhibition of the Prostaglandin synthetase pathway [3] and, therefore, occurs mostly secondary to maternal exposure to indomethacin [2, 4–6] or other non-steroidal anti-inflammatory

✉ Bindiya D. Chugh
bindiyadhingra237@gmail.com

[1] ADI Advanced Centre for Fetal Care, Sparsh Hospital, Yeshwanthpur, Bangalore, India


**Fig. 1** Doppler image showing high velocity flow in the ductus arteriosus of case 1

medications, isoxsuprine, fluoxetine or because of structural cardiac lesions. Other risk factors associated with ductal constriction are maternal ingestion of polyphenol-rich substances, such as herbal teas, orange and grape juice, dark chocolate, coffee, berries, soybeans, red apple, olive oil, peanuts, tomatoes and others with a high concentration of flavonoids [3, 7].

Idiopathic or isolated ductal constriction is a rare finding [8].

The pathophysiology results in fetal hemodynamic compromise due to increased afterload on the right ventricle causing tricuspid regurgitation, right ventricular hypertrophy and ultimately right ventricular failure. It may get further complicated and can result in hydrops, pulmonary hypertension and fetal demise [8–12].

Ultrasonographic findings that can help in the diagnosis of ductal constriction are as follows:

(1) S-shaped tortuosity of the ductal arch along with a distal ductal constriction in severe cases causing right ventricular hypertrophy and tricuspid regurgitation.
(2) High systolic and diastolic velocities in the DA constriction on spectral Doppler [5, 13].
    - Peak systolic velocity $> 1.4$ m/s.
    - Diastolic velocity $> 35$ cm/s.
    - Pulsatility index $< 1.9$.
(3) Dilated right ventricle.
(4) Right ventricular dysfunction (abnormal myocardial performance index).
(5) Tricuspid and pulmonary regurgitation.

The prognosis of ductal constriction depends on various factors like gestational age, rate of development of constriction, presence or absence of tricuspid regurgitation and amount of blood flowing through the right side of the heart [1].

Preventive measures include discontinuation of potential extrinsic agents and a close fetal surveillance which can result in improvement in the majority of cases.

Depending on the severity of the case during follow-up, mild cases may require fetal monitoring every 1–2 weeks prenatally and elimination of potential extrinsic agents. Postnatally, as pulmonary capillary bed relaxes with normal oxygen levels and there is shunting of blood across DA from left to right, eventually it begins to close. This helps in reducing the hemodynamic imbalance and all abnormal findings resolve within 3 weeks of postnatal life [14]. In

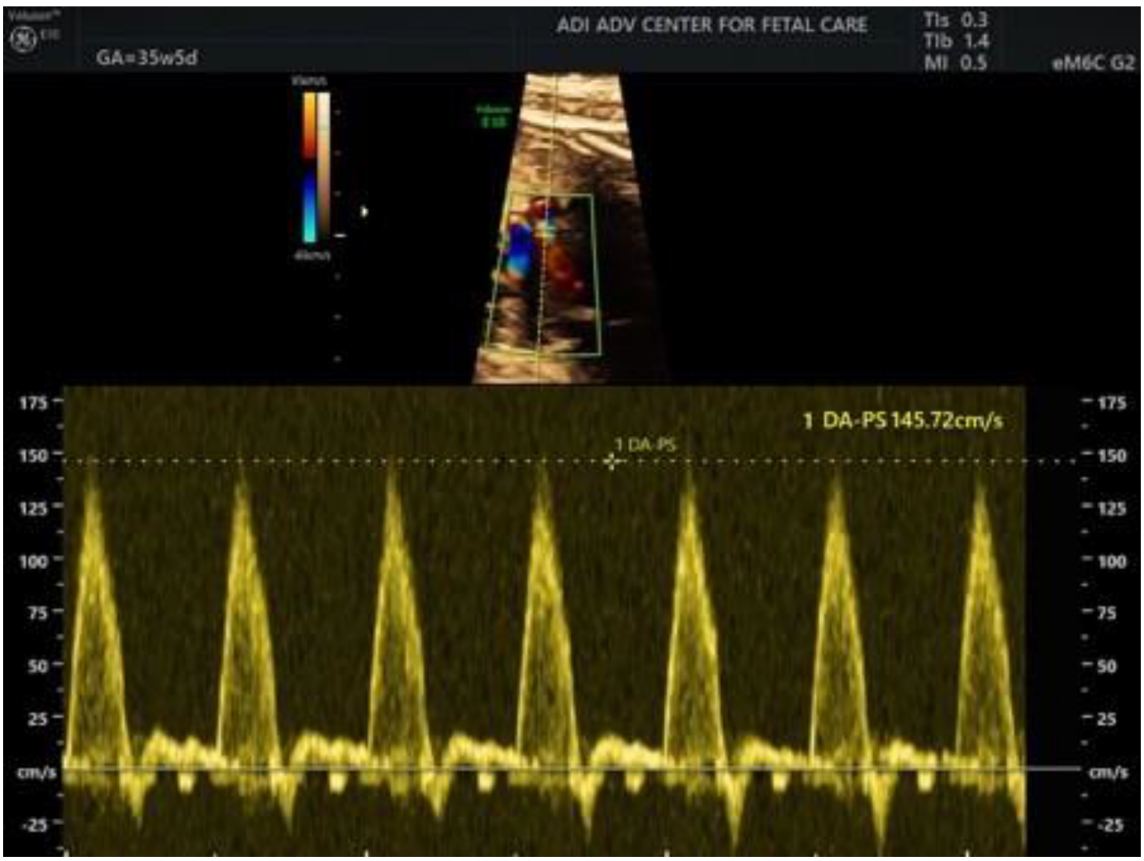


**Fig. 2** Spectral doppler showing high ductal flow velocity of case 2

cases of severe ductus arteriosus constriction with evidence of right heart compromise like right heart failure, hydrops, pulmonary hypertension, delivery by C-section is considered as delay in delivery may compromise fetal well- being and lead to intrauterine fetal demise.

We present case a series of fetal ductal constrictions and its outcome.

## Case 1

A 24 year old woman, G2P1 was referred for fetal echocardiography at 30 + 5 weeks of gestation because of abnormal looking ductal arch. The patient gave a history of pain in the abdomen 15 days back for which she was advised oral Ibuprofen.

Fetal echocardiography revealed a normal 4 chamber view with normal size and shape. The 2 AV valves appeared normal. There were two great arteries arising normally from appropriate ventricles with a normal sized main pulmonary artery and aortic root. Pulmonary and aortic valves looked normal. The aortic arch was normal in size and location but the ductal arch showed narrowing. On Color Doppler, a tortuous 'S' shaped ductus was seen. On Pulse Doppler, a ductal velocity of 1.0 m/s was observed. Flow velocity waveforms of the 2 great arteries were found to be within normal limits and no TR was noticed. A diagnosis of S-shaped DA with mild narrowing was made and a follow up examination was arranged.

A repeat examination was performed at 33 + 4 weeks of gestation. On greyscale, the right atrium and right ventricle were normal. No right ventricular dilatation was noted.TR was noted. DA was S-shaped and significant constriction was seen with the arterial duct measuring 3.9 mm wide, post constriction dilatation of 6.5 mm and a ductal velocity of 1.5 m/s and early systolic TR with regurgitant jet velocity up to 90 cm/s. In spite of the findings, fetal growth was within normal range and there was no evidence of fetal hydrops. The patient was asked to follow up at 35 weeks again. Findings were consistent with TR up to 100 cm/s (Fig. 1).

The patient was delivered at 36 weeks after preterm premature rupture of membranes. A healthy live male fetus of 2.25 kg was born with Apgar score of 9 and 10 at 1 min and 5 min respectively.The baby was discharged on day 6. Postnatal echo was done and was found unremarkable.

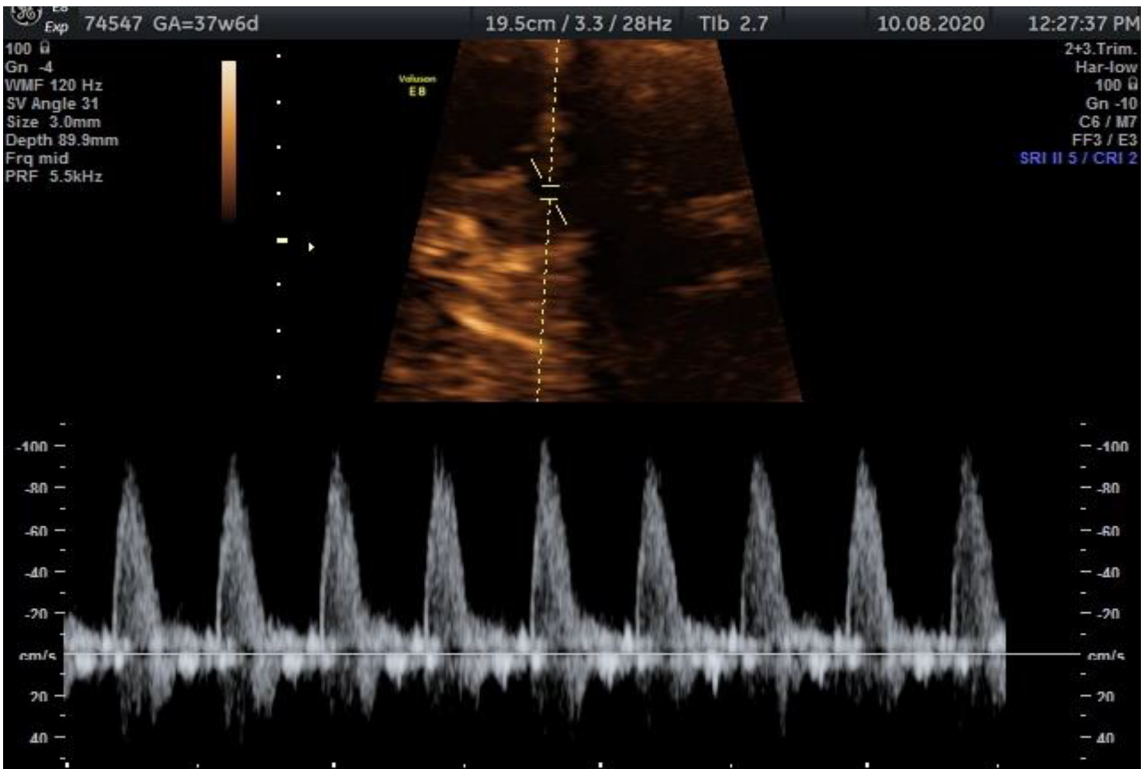


**Fig. 3** Shows normal ductal waveform on follow up of case 2

## Case 2

A 33 year old G3P1A1 came to our centre for a routine ultrasound examination for the first time at 35 + 5 weeks with no significant personal and family history.

2D examination revealed normal cardiac anatomy and outflow tracts but a narrow ductus arteriosus. No chamber discrepancy or TR was found. Spectral Doppler imaging confirmed high diastolic flow velocities with a pattern consistent with ductal constriction (Fig. 2).

The patient confirmed use of topical NSAIDs for intermittent back pain throughout the pregnancy including 48 h before the scan.

In view of the findings, the patient was asked to stop using analgesics and to follow up after 2 weeks. Ultrasound examination showed a normal waveform of the ductus arteriosus with no TR after stopping the drug (Fig. 3).

The patient was delivered vaginally at 38 weeks with a healthy female baby of 2.8 kg with an Apgar score of 9 and 10 at 1 min and 5 min respectively and was discharged on day 3 post delivery. Neonatal echocardiography was done before discharge and was normal.

## Case 3

A 29 years, primigravida was referred for a second opinion at 35 + 3 weeks for the ductal arch. No significant personal or family history was forthcoming.

On 2D imaging and grey scale, right side of the heart looked slightly larger than the left side. The coronary sinus was dilated. The 3 vessel view showed a persistent left superior vena cava(PLSVC). Fetal echocardiography showed ventricular chamber size discrepancy with right side dominance. The right atrium and right ventricle looked slightly larger than the left sided heart. Color Doppler showed dilated and tortuous duct with turbulent flow and narrowing in proximal duct with diastolic peak velocity of 1.4 m/s. It also revealed a holosystolic TR with velocities up to 90 cm/s (Figs. 4, 5).

Patient was asked to follow up to observe for fetal hydrops or any other markers of right heart failure. At 37 + 2 weeks, examination showed similar findings consistent with significant ductal constriction and no evidence of hydrops. The case was discussed with the obstetrician, cardiologist, cardiac surgeon and neonatologist and patient was planned for delivery. Delivery was done by C-section and a 2.4 kg female was born with Apgar score of 7 and 8 at 1 min and 5 min respectively. At birth, baby showed signs of tachypnea and low oxygen tension. Neonatal echocardiography showed mild right ventricular

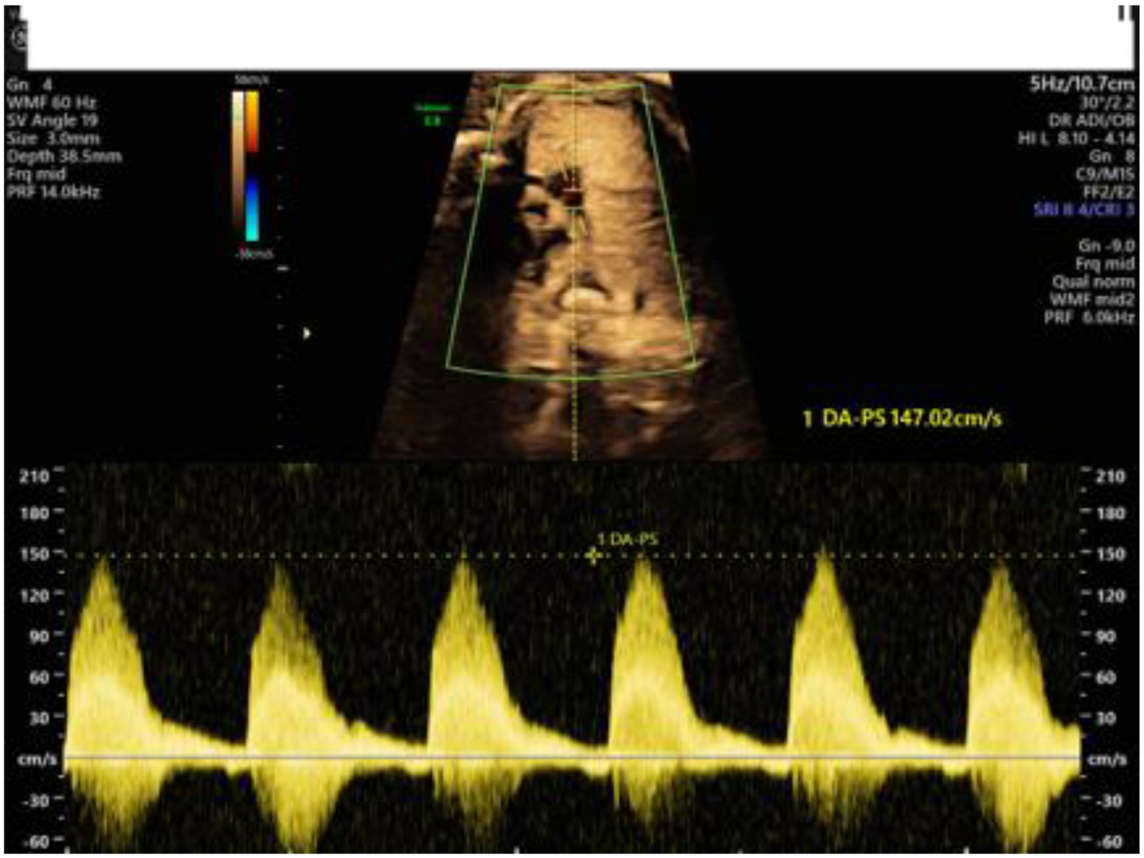


**Fig. 4** Spectral doppler showing peak systolic velocity of 1.4 m/s in case 3

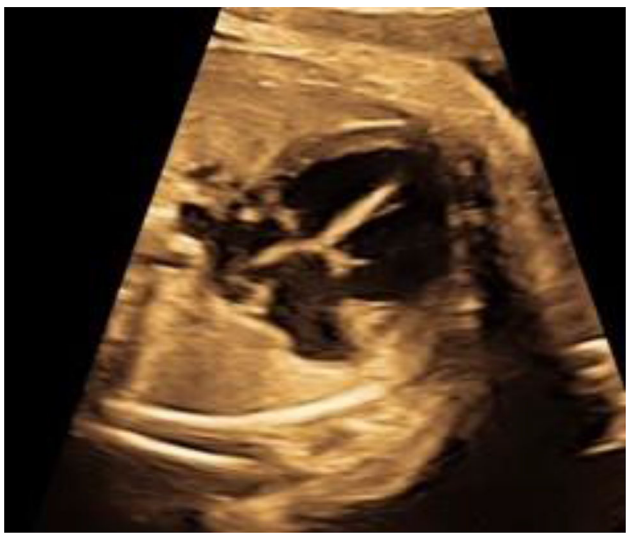

**Fig. 5** 4 chamber view showing enlarged right atrium and right ventricle with regurgitant flow through tricuspid valve

hypertrophy with trivial tricuspid regurgitation. No ductus was seen on

2-D and Color Doppler imaging. Baby was given supplemental oxygen and was discharged on day 3 of postnatal life. Repeat echocardiography done after 1 month showed that the right ventricle was normal in size and there was no tricuspid regurgitation

## Case 4

31 year old woman, G2A1 came to our centre for routine growth scan at 32 weeks of gestation. Pregnancy was found uneventful till date. There was no significant family or personal history. On 2D examination of fetal heart, cardiac anatomy and outflow tracts were found normal. TR was noted in 4 chamber view and tortuous S-shaped ductal arch with a ductal constriction was seen in 3 V-view with arterial duct measuring 4.6 mm, post-constriction dilatation of duct measuring 7.1 mm. Pulse Doppler revealed significantly increased ductal peak systolic velocity of 1.5 m/s and early systolic TR with jet velocity up to 90 cm/s. There was no evidence of right ventricular hypertrophy or right ventricle outflow tract obstruction and no other structural lesion noted to account for narrowing at distal ductus arteriosus (Fig. 6).

As a result, a repeat fetal echocardiography was performed after 1 week(34 weeks) which revealed moderate to severe right ventricular hypertrophy with thickened right

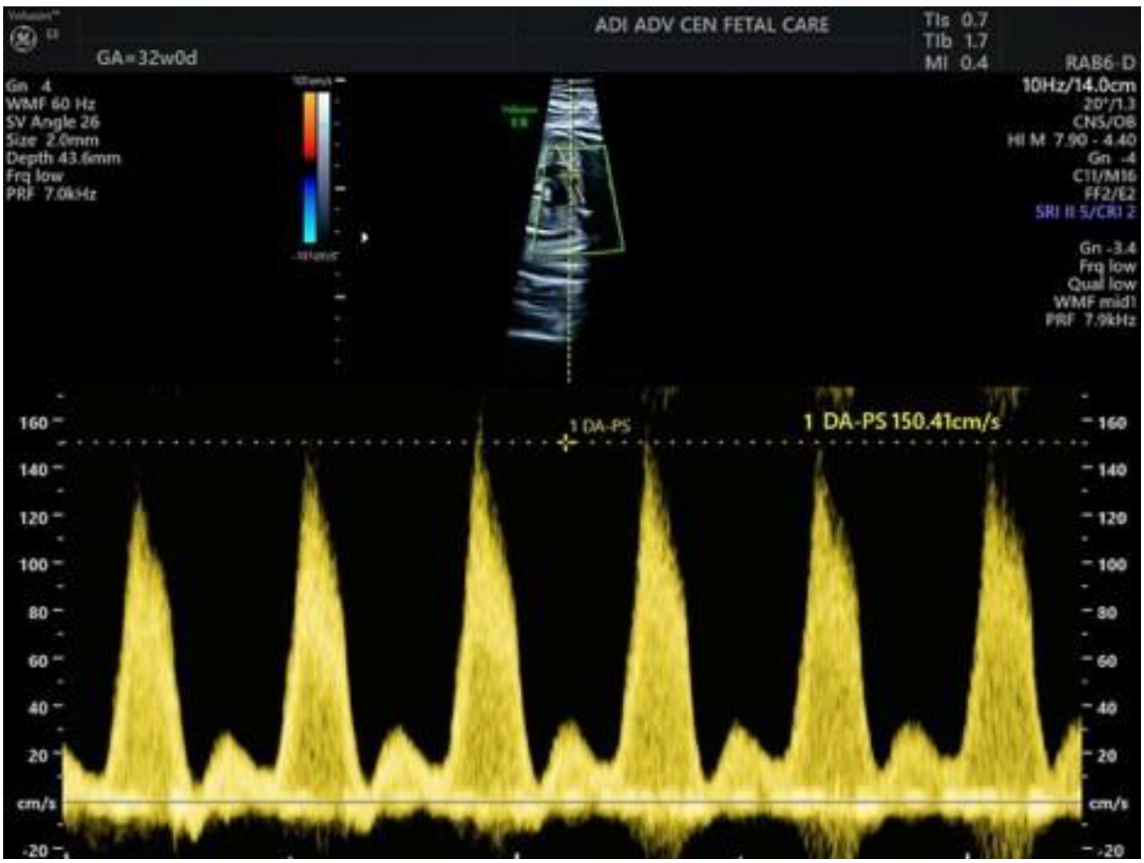


**Fig. 6** Pulse doppler showing high ductal peak systolic velocity of 1.5 m/s of case 4

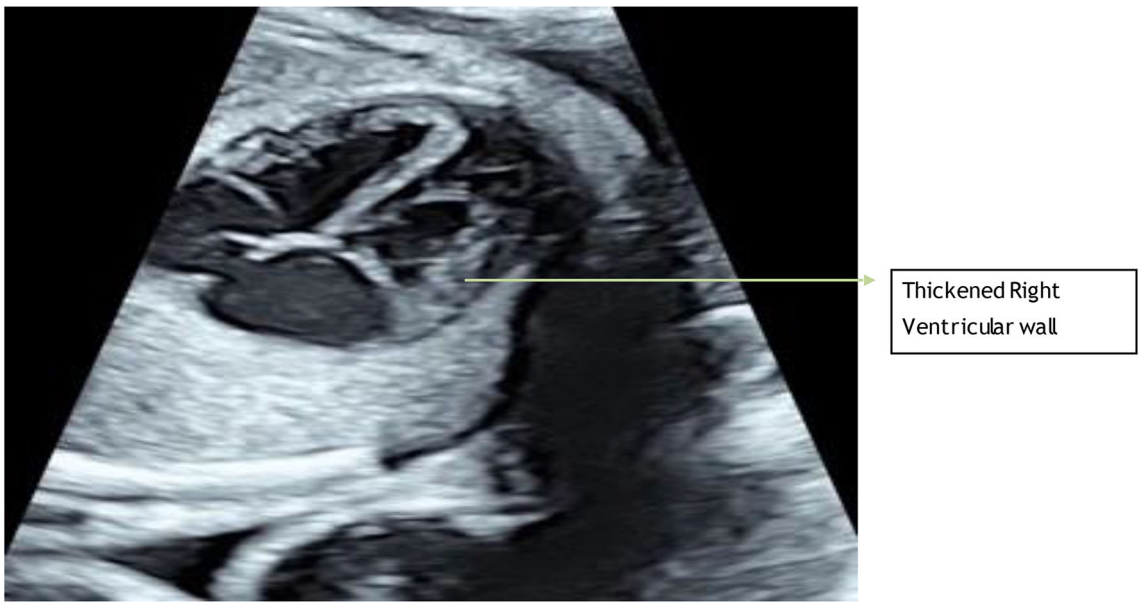


**Fig. 7** 4 chamber view showing thickened right ventricular wall

ventricular wall and diminished intraventricular volume. It was also associated with holosystolic TR of 110 cm/sec and a tortuous S-shaped ductal constriction with increased peak systolic velocity of 2 m/s (Fig. 7).

Patient was scheduled for regular ultrasound surveillance to observe for fetal hydrops. No evidence of hydrops was noted throughout the test of the pregnancy. The patient was induced at $37 + 5$ weeks of gestation. A female baby weighing 2.6 kg was born by C- section. The apgar score was 7 and 8 at 1 min and 5 min respectively. Baby showed signs of tachypnea, grunting, chest retraction and low oxygen saturation. Neonatal echocardiography showed a markedly dilated right ventricle suggestive of right ventricular hypertrophy with severe tricuspid regurgitation of 100 cm/s and the ductus was found closed.

The neonate was kept on mechanical ventilation for 2 days and was discharged on the 10th day of neonatal life after recovery. Repeat echocardiography was performed after 1 month and the right ventricle was normal with presence of physiological tricuspid regurgitation.

## Discussion

In this case series analysis, we retrieved and discussed 4 cases of fetal ductus arteriosus constriction, out of which Case 1 and 2 described constriction following maternal use of NSAIDs, whereas Case 3 and 4 were idiopathic. Fetal DA constriction is rare but important because it is associated with significant morbidity and mortality [1].

The DA connects pulmonary artery and descending aorta and allows shunting of the blood from the right ventricle to the aorta which is essential in fetal circulation. Normaly, it starts to close within the first few hours after birth and gets completed by 72 h of age to establish the adult circulation pattern.

Ductal constriction is defined as significant narrowing of the patent DA during pregnancy due to inhibition of prostaglandin synthesis pathway which results in fetal hemodynamic compromise leading to hypertrophy of pulmonary arteries and pulmonary hypertension [3]. DA constriction can occur spontaneously or secondary to use of certain drugs.

NSAIDs are widely used drugs to treat symptoms like inflammation and pain. It has been reported that the risk of DA constriction increases if NSAIDs are used in the 3$^{rd}$ trimester. NSAIDs may lead to ductal arteriosus constriction but are usually reversible after discontinuation of the drug. However, NSAIDs can affect renal function and cause decreased renal perfusion which leads to decrease urine output and oligohydraminos. But in our cases, no oligohydraminos was noted.

Pregnant women should be counselled about the potential side effects on the fetus following the use of NSAIDs whether orally or topically especially in the 3rd trimester, although no underlying cause of ductal constriction is still clear [7].

In a cohort of 20 cases of intrauterine DA constriction, NSAIDs usage as a precipitant was identified in only 30% cases [15].

Drugs other than NSAIDs like fluoxetine, isoxsuprine have also been reported recently to cause ductal arteriosus constriction [16].

Close fetal surveillance should be considered if these drugs are taken in late pregnancy. Patient should be advised to stop taking the drug for the rest of the pregnancy. Patients should avoid taking foods such as cranberry, dark chocolate, tea, coffee, herbal teas etc. Based on this, a study was published in August, 2009 by S. Sridharan which reported 2 cases of DC after ingestion of Camomile tea and showed complete resolution of Ductal constriction 1 week after stopping of tea [7].

Out of our 2 cases of idiopathic fetal DA constriction, case case 4 showed severe DA constriction with TR and case 3 demonstrated significant DA constriction with right ventricular dilatation, hypertrophy and holosystolic TR, although no fetal hydrops was noted. These cases remain idiopathic as there was no identifiable underlying cause and mother denied any history of NSAIDs usage. There are almost 20 cases of idiopathic ductal constriction according to a Korean study in 2013 which includes 13 cases of ductal constriction of variable degree associated with significant TR as a common finding [1].

Ductal constriction is usually, but not always reversible after withdrawl of causative agents. With reference to management, fetuses with ductal constriction associated with complications like right ventricular failure and other signs of fetal distress such as hydrops are managed by immediate delivery if they are near term. However, if the fetus is not in distress, it can be followed with close surveillance. If a premature fetus is in distress, a decision for delivery is to be taken, outweighing the fetal risk of prematurity and postnatal complications.

Postnatal prognosis seems to be good in mild as well as significant cases of ductal constriction associated with right heart abnormalities as right heart abnormalities resolve in a couple of weeks, although pulmonary hypertension and RV failure are major concerns postnatally [1].

## Conclusion

- DA constriction occurs due to imbalance of prostaglandins in the intrauterine environment leading to dilatation and hypertrophy of the right side of the heart, tricuspid regurgitation, cardiac failure, hydrops and intrauterine fetal death in severe cases.
- The most common cause is administration of maternal NSAIDs after 27 weeks of gestation, which produces a dose-dependant but reversible constriction.

- Structural anomalies associated with DA constriction include tetralogy of Fallot and truncus arteriosus.
- A peak systolic velocity of more than 1.4 m/s with a persistent diastolic peak flow velocity of greater than 0.35 m/s and a PI of less than 1.9 on fetal echocardiography is suggestive of ductal constriction.
- Treatment includes discontinuation of NSAIDs or anti-inflammatory drugs. Mild cases require close fetal surveillance and severe cases may need urgent delivery.
- Precautions include avoidance of foods like tea, coffee etc. and avoidance of drugs like NSAIDs, fluoxetine and isoxsuprine.

#### Compliance with Ethical Standards

**Conflict of interest** The article has no conflict of interest.

## References


1. Choi EY, Li M, Choi CW, Park KH, Choi JY. A case of progressive ductal constriction in a fetus. Korean Circ J. 2013;43(11):774–81.
2. Kohler HG. Premature closure of the ductus arteriosus (P.C.D.A.): a possible cause of intrauterine circulatory failure. Early Hum Dev. 1978;2:15–23.
3. Zielinsky P, Piccoli AL Jr, Manica JL, Nicoloso LH. New insights on fetal ductal constriction: role of maternal ingestion of polyphenol- rich foods. Expert Rev Cardiovasc Therapy. 2010;8(2):291–8. https://doi.org/10.1586/erc.09.174.
4. Truter PJ, Franszen S, van der Merwe JV, Coetzee MJ. Premature closure of the ductus arteriosus causing intra-uterine death. A case report. S Afr Med J. 1986;70(9):557–8.
5. Huhta JC, Cohen AW, Wood DC. Premature constriction of the ductus arteriosus. J Am Soc Echocardiogr. 1990;3(1):30–4.
6. Tumbarello R, Pisu F, Pisano E, Puddu R, Timely Bini RM, et al. Detection of premature closure of the ductus arteriosus in a full-term fetus. Important role of fetal echocardiography. Minerva Ginecol. 1999;51(5):197–201.
7. Sridharan S, Archer N, Manning N. Premature constriction of the fetal ductus arteriosus following the maternal consumption of chamomile herbal tea. Ultrasound Obstet Gynecol. 2009;34:358–9.
8. Mielke G, Peukert U, Krapp M, Schneider-Pungs J, Gembruch U. Fetal and transient neonatal right heart dilatation with severe tricuspid valve insufficiency in association with abnormally S-shaped kinking of the ductus arteriosus. Ultrasound Obstet Gynecol. 1995;5:338–41.
9. Gewillig M, Brown SC, De Catte L. Premature fetal closure of the arterial duct: clinical presentations and outcome. Eur Heart J. 2009;30:1530–6.
10. Souter D, Harding J, McCowan L, O'Donnell C, McLeay E, Baxendale H. Antenatal indomethacin: adverse fetal effects confirmed. Aust NZ J Obstet Gynaecol. 1998;38:11–6.
11. Weichert J, Hartge DR, Axt-Fliedner R. The fetal ductus arteriosus and its abnormalities: a review. Congenit Heart Dis. 2010;5:398–408.
12. Downing GJ, Steil E, Breuer J, Goelz R. Pulmonary vascular changes associated with idiopathic closure of the ductus arteriosus and hydrops fetalis. Pediatr Cardiol. 1994;1:71–5.
13. Tulzer G, Gudmundsson S, Sharkey AM, Wood DC, Cohen AW, Huhta JC, et al. Doppler echocardiography of fetal ductus arteriosus constriction versus increased right ventricular output. J Am Coll Cardiol. 1991;18:532–6.
14. Trevett TN Jr, Cotton J. Idiopathic constriction of the fetal ductus arteriosus. Ultrasound Obstet Gynecol. 2004;23:517–9.
15. Luchese S, Manica JL, Zielinsky P. Intrauterine ductus arteriosus constriction: analysis of a historic cohort of 20 cases. Arq Bras Cardiol. 2003;81:405–10.
16. Lopes LM, Carrilho MC, Francisco RP, Lopes MA, Krebs VL, Zugaib M. Fetal ductus arteriosus constriction and closure: analysis of the causes and perinatal outcome related to 45 consecutive cases. J Matern Fetal Neonatal Med. 2015;29(4):1–8.