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# Comparison of Diagnostic Markers of Aortic Coarctation in Prenatal and Postnatal Echocardiography

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## ABSTRACT

***Background:*** The prenatal diagnosis of coarctation of aorta (CoA) remains a major challenge, as the false-positive diagnosis is fairly common. The purpose of this study was to find some useful prenatal sonographic markers compatible with the postnatal diagnosis of CoA.

***Methods:*** The study included fetuses suspected of CoA in the second and third-trimester ultrasound tests. All cases were examined by fetal echocardiography at a single ultrasound clinic between 2019 and 2020. The proportion of right and left ventricular size was assessed and ductal/isthmus diameter ratio was measured. A comparison was drawn between the results of neonates with neonatal CoA and neonates without CoA.

***Results:*** Of 20 fetuses with suspected prenatal CoA, 3 (15%) had neonatal CoA. The mean ductal/isthmus ratio was significantly higher in the neonates with CoA (1.96 vs. 1.46; p< 0.001). The diagnostic power of ductal/isthmus ratio to detect CoA with a cut point of 1.53 had a sensitivity and specificity of 100% and 70.6%, respectively, a positive and negative predictive value of 37.5% and 100%, respectively, and an overall accuracy of 75%.

***Conclusion:*** The ductal/isthmus ratio diameter and ventricular disproportion are significant sonographic markers for the prenatal diagnosis of CoA, and the ductal/isthmus ratio has high sensitivity and specificity compared to postnatal findings.

***Keywords:*** Aortic coarctation, Fetal echocardiography, Prenatal diagnosis

## Introduction

Coarctation of the aorta (CoA) is one of the most frequent congenital heart defects that account for about 8% of all cardiac defects (1). The incidence of CoA was estimated at 4/10000 neonates (2). Despite advancements in screening techniques and fetal echocardiography, prenatal and neonatal diagnosis of CoA is still difficult, and linked to high morbidity and mortality (3). True positive detection rates of CoA in prenatal screening have already been reported to be less than 50% (4).

Prenatal diagnosis of CoA is particularly important because it can significantly reduce the risk of fatal complications, such as aortic rupture, endocarditis, and intracranial hemorrhage, by ensuring required management such as delivery in a center equipped with the neonatal intensive care unit (NICU), timely treatment, or surgery (5). Although hypoplastic aortic valve, ventricular septal defect, transverse arch hypoplasia, and isthmic hypoplasia are all proven risk factors for CoA, their predictive power of surgery has been estimated to be less than 65% (4,6–8).

Several studies have attempted to find some prenatal sonographic markers for the prediction

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of neonatal CoA, finding that these criteria alone have a low diagnostic value, which is even less accurate in the third trimester of pregnancy (9–12). Therefore, it is essential to have some prenatal sonographic indicators that can properly identify high-risk fetuses for neonatal CoA and are easily recognized by routine prenatal screening exams. In the present study, we investigated the diagnostic value of various ultrasound markers in the prenatal diagnosis of neonatal CoA, given the relevance of prenatal diagnosis of neonatal CoA and the current diagnostic challenges.

## Methods

A prospective cohort study was conducted on twenty pregnant women with a gestational age of 18 to 38 weeks whose fetuses were suspected of aortic coarctation. They were referred to a tertiary ultrasound clinic from March 2019 to March 2020. The sample size was calculated as described in the study of E Gómez-Montes. They reported a sensitivity of 76% for the cut point of 1.6 or higher for the ductal/isthmus ratio. The sample size was calculated using the Cochran formula with CI=f 95%. The sampling was conducted using the convenience sampling method. The inclusion criterion was a gestational age of 18 to 28 weeks. The mothers who could not be reached during the study or their fetuses had other congenital heart diseases were excluded.

All fetuses were examined by a team of specialists including a radiologist and a pediatric cardiologist. The scan was carried out by a Samsung WS80 system (South Korea 2018) equipped with 4-7 MHz curvilinear transducer. In the four-chamber view of fetal echocardiography, the transverse diameter of the right and left ventricles at the atrioventricular valve was measured and ventricular disproportion was assessed. Furthermore, in the three-vessel tracheal view (3VT), isthmus diameter and ductal/isthmus diameter ratio (D/I) were measured.

The fetuses received follow-up ultrasounds until birth. After delivery, all newborns were studied by echocardiography in a referral center. Abnormal findings of prenatal and postnatal echocardiograms were reviewed and compared, and finally the diagnostic accuracy of prenatal ultrasound was determined.

The study checklist, including demographic information and other variables, was completed by the pediatric cardiologist. The data was analyzed by IBM SPSS software version 22.0 (SPSS Inc., Chicago, IL, USA). The normality of data distribution was first assessed using the Shapiro–Wilk test and the Mann-Whitney test was used for nonparametric data. P-value<0.05 was considered statistically significant. Roc curve and Cohen's kappa coefficient were used to determine the cut point of the ductal/isthmus ratio.

The patients completed an informed consent form. Moreover, the study protocols, consistent with Helsinki Declaration guidelines, were fully approved by the Ethics Committee of the Islamic Azad University of Medical Sciences(#IR.IAU.MSHD.REC.1398.043).

## Results

Twenty fetuses (12 males and 8 females) suspected of CoA were enrolled in the study. The mean age of the pregnant women was 31.55 ± 5.24 years (22-45 years) and the mean gestational age was 26.05 ± 7.63 weeks (18-38 weeks). Of the 20 fetuses, 3 (15%) had neonatal CoA (true-positive group), and 17 (85%) did not have neonatal CoA (false-positive group).

As illustrated in Table 1, there were no significant differences between CoA and non-CoA groups in terms of maternal age (p=0.682), gestational age (p= 0.078), sex (p= 0.242), consanguineous marriage (p= 0.074), and additional cardiac anomalies (p= 0.14).

The right ventricle was dominant in 100% of neonates in the CoA group, whereas it was dominant only in 94.1% of neonates in the non-CoA group. Nevertheless, the difference was not statistically significant (p=1). The mean ductal/isthmus ratio was significantly higher in neonates with CoA than those without CoA (p< 0.001).

The ROC analysis of the ductal/isthmus ratio revealed an AUC of 0.902 (CI=95%, 0.72–1.00; p< 0.05). The optimum cut-off point in the diagnosis of CoA, with the highest sensitivity and specificity, is 1.53. The diagnostic power of ductal/isthmus ratio in detecting CoA at a cut-off point of 1.53 had sensitivity and specificity of 100% and 70.6%, respectively, a positive and negative predictive value of 37.5% and 100%, respectively, and an overall accuracy of 75% (Table 2).

The overall diagnostic accuracy of the ductal/isthmus ratio in the diagnosis of CoA was 100% in women above 30 years of age, and 44.4% in women younger than 30 years. In addition, the overall accuracy of the ductal/isthmus ratio in the diagnosis of CoA was 75% in both boys and girls. According to the gestational age, the overall accuracy of the ductal/isthmus ratio in the diagnosis of CoA was 100% (p= 0.001) below 30 weeks and 37.5% above 30 weeks.

**Table 1**. Different parameters in fetuses with/without postnatal CoA

| Characteristics | Postnatal CoA | | P-value |
|---|---|---|---|
| | Yes (N: 3) | No (N: 17) | |
| Maternal age (year) | 32.66 ± 4.51 | 31.35 ± 5.47 | 0.682 |
| Gestational age (weeks) | 19.33 ± 2.31 | 27.23 ± 7.65 | 0.078 |
| Gender (Male) | 3 (100%) | 9 (52.9%) | 0.242 |
| Consanguineous marriage | 0 (0%) | 11 (64.7%) | 0.074 |
| Cardiac disease in a previous child | 1 (33.3%) | 0 (0%) | 0.15 |
| Additional cardiac anomalies | 2 (66.7%) | 3 (17.6%) | 0.14 |
| Ventricular disproportion | 3 (100%) | 16 (94.1%) | 1 |
| Ductal/isthmus ratio | 1.96 ± 0.41 | 1.46 ± 0.12 | < 0.001 |

**Table 2.** The diagnostic value of the ductal/isthmus ratio in the diagnosis of CoA according to the study variables

| Variable | | True-positive | False-positive | True-negative | False-negative | Sensitivity | Specificity | PPV | NPV | Positive probability | Negative probability | Overall accuracy | Kappa | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | Coefficient | P-value |
| Total | | 3 | 5 | 12 | 0 | 100% | 70.6% | 37.5% | 100% | 3/4 | 0 | 75% | 0.419 | 0.021 |
| Age | <30 | 1 | 5 | 3 | 0 | 100% | 37.5% | 16.7% | 100% | 1/6 | 0 | 44.4% | 0.118 | 0.453 |
| | >30 | 2 | 0 | 9 | 0 | 100% | 100% | 100% | 100% | - | 0 | 100% | 1 | 0.001 |
| Sex | Boy | 3 | 3 | 6 | 0 | 100% | 66.7% | 50% | 100% | 3 | 0 | 75% | 0.5 | 0.046 |
| | Girl | 0 | 2 | 6 | 0 | 0 | 75% | 0 | 100% | 0 | 1/33 | 75% | - | - |
| Gestational age | <30 | 3 | 0 | 9 | 0 | 100% | 100% | 100% | 100% | - | 0 | 100% | 1 | 0.001 |
| | >30 | 0 | 5 | 3 | 0 | 0 | 37.5% | 0 | 100% | 0 | 2/66 | 37.5% | - | - |
| Consanguineous marriage | No | 3 | 2 | 4 | 0 | 100% | 66.7% | 60% | 100% | 3 | 0 | 77.7% | 0.571 | 0.058 |
| | Yes | 0 | 3 | 8 | 0 | 0 | 72.7% | 0 | 100% | 0 | 1/37 | 72.7% | - | - |
| Cardiac disease in previous children | No | 2 | 5 | 12 | 0 | 100% | 70.6% | 28.6% | 100% | 3/4 | 0 | 73.6% | 0.336 | 0.05 |
| | Yes | 1 | 0 | 0 | 0 | 100% | - | 100% | - | - | - | 100% | - | - |

## Discussion

This study was conducted to evaluate the diagnostic value of prenatal ultrasound markers in predicting the neonatal diagnosis of CoA. The CoA diagnosis was confirmed postnatally in three cases (15%) out of 20 fetuses. There was no significant difference between neonates with and without CoA in terms of maternal age, neonatal sex, gestational age, consanguineous marriage, cardiac disease in previous children, additional anomalies, and ventricular disproportion, but the mean ductal/isthmus ratio was significantly higher in patients with CoA than in patients without CoA. The results demonstrated that the diagnostic power of ductal/isthmus ratio in detecting CoA at a cut-off point of 1.53had sensitivity and specificity of 100% and 70.6%, respectively, a positive and negative predictive value of 37.5% and 100%, respectively, and overall accuracy of 75%.

In a study by Gomez-Montes et al. on predicting CoA in the second trimester of pregnancy, 85 fetuses were diagnosed to be suspected of prenatal CoA based on sonographic findings (12). This study was performed in two groups. The first group had a gestational age of ≤28 weeks, of whom 32 (80%) were diagnosed with neonatal CoA, whereas the second group had a gestational age of >28 weeks, of whom 9 (20%) were diagnosed with neonatal CoA (12). In the present study, all fetuses with neonatal CoA had a gestational age of below 20 weeks. The normal neonates and the postnatal CoA group were significantly different in terms of gestational age. Although P-value was not statistically significant, it might influence results and should be considered in future studies. It is suggested to divide cases into two groups according to gestational age.

In a study by Mărginean et al., 32 fetuses with a gestational age of 32 to 39 weeks were evaluated for ventricular disproportion, aortic diameter, and ductal/isthmus diameter for the diagnosis of fetal CoA (13).

The cut-off point of the ductal/isthmus ratio for CoA detection was estimated at 1.4, which is close to the cut-off point obtained in the present study (1.53). Both findings suggest the importance of this ultrasound indicator in suspicious fetuses.

In the same vein, Anuwutnavin et al. evaluated 35 fetuses with prenatal suspicion of CoA, of whom the diagnosis of neonatal CoA was confirmed in 25% of cases (14). Also, in our study, 15% out of 20 fetuses with prenatal suspicion of

CoA had neonatal CoA. These results are aligned with the study by Buyens et al., who reported that despite growing research on approaches for prenatal detection of CoA, the ultrasound markers remain a challenge to correct diagnosis of CoA in prenatal life (15).

In a similar study, Jowett et al. used four sonographic parameters for the assessment of fetuses suspected of CoA, including isthmus diameter, isthmus/ductal ratio, visualization of CoA shelf, and the isthmus flow disturbance (7). They concluded that a combination of these four sonographic parameters improves diagnostic accuracy to 86% for the detection of true neonatal that requires perinatal surgery (7). Although only one of these markers was investigated in this study, the diagnostic accuracy calculated is similar to that of the above study.

## Conclusion

According to our findings, only 15% of fetuses with prenatal suspicion of CoA had neonatal CoA and the ductal/isthmus ratio in patients with CoA was significantly higher than those without CoA. The diagnostic power of ductal/isthmus ratio in the detection of CoA at a cut-off point of 1.53, had sensitivity and specificity of 100% and 70.6%, respectively, a positive and negative predictive value of 37.5% and 100%, respectively, and overall accuracy of 75%. Therefore, although diagnostic accuracy (particularly the positive predictive value and specificity) is not satisfactory, fetal ultrasound is promising for the prenatal detection of CoA and further studies are warranted to search for new ultrasound parameters with a larger sample size.

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## Conflicts of interest

None

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