Obstetrics; *Maternal-Fetal Medicine and Perinatology*

Importance of Aberrant Right Subclavian Artery Detection During Second Trimester Ultrasound Examination in Low-Risk Population

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ABSTRACT

OBJECTIVE: Aberrant right subclavian artery, which is detected in 1-1.5% of the population, is considered an anatomical variant. Aberrant right subclavian artery is usually not symptomatic, but can sometimes lead to dysphagia due to esophageal compression. On the other hand, it has been found that it has accompanied some fetal anomalies in the last two decades. Although aberrant right subclavian artery is seen at a rate of 1-1.5% in normal chromosomal fetuses, it is seen at a rate of 19-36%, especially in fetuses with Down syndrome.

STUDY DESIGN: Our study was carried out in the Department of Obstetrics and Gynaecology at Ankara University Faculty of Medicine between the dates of January 2017-January 2020. Pregnant women have had their detailed ultrasonography at our clinic and who were between 18th-24th gestational weeks were included. Amniocentesis was performed on the patients who have accepted, and genetic results were followed up. The patients who did not accept were followed up until after birth, and genetic testing was requested for babies suggestive of anomaly.

RESULTS: Our study included 6205 patients who underwent detailed ultrasonography in our clinic between January 2017 and June 2020. Our detailed ultrasonography application week was between 16-24 weeks. During this period, aberrant right subclavian artery was detected in 47 of our patients. The detection rate of ARSA in the normal population in our study was 0.7% (46/6205). While aberrant right subclavian artery was the only ultrasonographic finding in 28 patients, extra anomalies were observed in 18 patients. Down syndrome was detected in four fetuses,

CONCLUSION: We did not find any chromosomal anomalies in any of the patients with isolated aberrant right subclavian artery. Therefore, we do not recommend invasive intervention in patients with isolated aberrant right subclavian artery. On the other hand, our study confirmed that aberrant right subclavian artery screening should be a part of a detailed fetal ultrasonographic examination. Further studies with larger patient groups are needed.

Keywords: Aberrant right subclavian artery, Down syndrome, Prenatal diagnosis, Ultrasonography

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Introduction

In the branching pattern of the aortic arch, the right subclavian artery arises from the right brachiocephalic artery. According to the hypothetical model, there are two aortic arches at the beginning of the embryological period. Then the connection between the right carotid common artery (RCCA) and right subclavian artery (RSA) regresses and a normal aortic arch is formed. If the proximal part regresses instead of the distal part, an aberrant right subclavian artery (ARSA) is developed and it separates from the aorta as the fourth vessel after the left subclavian artery (LSA) and runs to the posterior

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of the trachea and esophagus, then turns towards the right shoulder. This condition is called ARSA (1).

Aberrant right subclavian artery can be detected during a routine antenatal ultrasound (USG) examination and is more easily identified if the Doppler USG mode is used (2,3). It has been shown ARSA is detected in the first and second trimesters at rates respectively 82-84% and 95-98% (4,5).

Aberrant right subclavian artery, which is detected in 1-1.5% of the population, is considered an anatomical variant. ARSA is usually not symptomatic, but can sometimes lead to dysphagia due to esophageal compression (6,7). On the other hand, it has been found that it has accompanied some fetal anomalies in the last two decades. Although ARSA is seen at a rate of 1-1.5% in normal chromosomal fetuses, it is seen at a rate of 19-36%, especially in fetuses with Down syndrome (8). For example, in fetuses with trisomy 21, ARSA was first identified by Chaoui et al. in 2005 (3). In their study, fourteen fetuses between 18 to 33 weeks of gestation, known to have trisomy 21, were evaluated and it was found that the right subclavian artery was aberrant in five (35.5%). In fetuses with trisomy 21, the incidence of ARSA is increased (30-40%) (9). Postnatally, the aberrant right subclavian artery has a 1-2% prevalence in autopsies. The incidence of ARSA has been reported as 3% in cases of congenital cardiac defects (10).

This study aims to reveal the prevalence of ARSA in the low-risk patient population in the second trimester and to evaluate the relationship of ARSA with aneuploidies and accompanying anomalies.

Material and Method

We designed this study as a prospective cohort. We included fetuses with normal and abnormal karyotypes with ARSA in the low- and high-risk population.

Our study was carried out in the Department of Obstetrics and Gynaecology at Ankara University Faculty of Medicine between the dates of January 2017-January 2020. Pregnant women have had their detailed ultrasonography at our clinic and who were between 18th-24th gestational weeks were included. Between 2017 and 2020, 9724 pregnant women were examined at least once in our center, and their USG reports and newborn documents were collected. Approximately 157 pregnancies were excluded. Because they had at least one of the criteria such as chronic maternal disease, familial heart disease, drug use, or high risk in the first-trimester screening test. The study was reviewed and approved by the ethics committee of Ankara University Faculty of Medicine (Ethics approval reference number: 437, date: 10.12.2021). All procedures were performed according to the Declaration of Helsinki. Written consent forms were obtained from the participants. Amniocentesis was recommended as a genetic diagnostic test for all pregnant women with ARSA.

Amniocentesis was performed on the patients who have accepted, and genetic results were followed up. The patients who did not accept were followed up until after birth, and genetic testing was requested for babies suggestive of anomaly. Two things were investigated: in fetuses with trisomy 21, it was investigated whether there are additional ultrasonographic markers suggestive of chromosomal abnormality and in fetuses, with ARSA it was investigated whether this is an isolated marker.

All ultrasonographic examinations and measurements were performed with the Voluson E8 Expert color Doppler ultrasonography device by five practitioners with at least 10 years of clinical experience. We have added RSA as part of routine second-trimester screening since 2015. Transabdominal ultrasonographic examinations were performed in the supine position, in a position where fetal movements are minimal and three-vessel trachea images could be obtained in the transverse plane. RSA was considered normal when the following criteria were met. 1) Three-vessel trachea view 2) RSA transition from the front of the trachea to the right shoulder 3) Arterial flow pattern on Doppler USG. The normal RSA view is shown in figure 1.

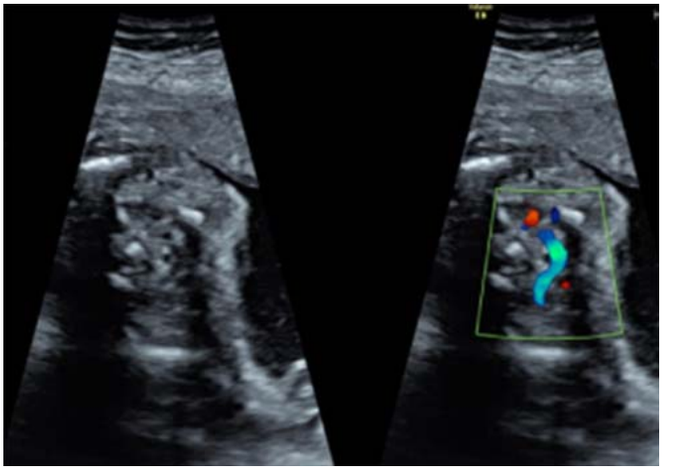

Figure 1: *Normal and Color Doppler axial image shows the course of the normal right subclavian artery (arrows) anterior to the trachea*

But the opposite is seen in ARSA as discussed below. First, three-vessel trachea and aortic arch images were taken in the transverse plane. By keeping the insonation angle below 45 degrees, the area where we expected the aberrant right subclavian artery was visualized. To prevent the azygos vein from mixing with the superior vena cava and ARSA, it was checked with Doppler ultrasonography whether the vein trace that we saw belonged to the artery. ARSA view is shown in figure 2. In the case of vein trace on Doppler, this was considered as azygos vein. It was done following the principles suggested by the International Society of Obstetrics and Gynaecology (ISUOG) (11). In fetuses with Trisomy 21 in whom ARSA was detected, it was examined whether it was an isolated finding and its association with other accompanying ultrasonographic findings.

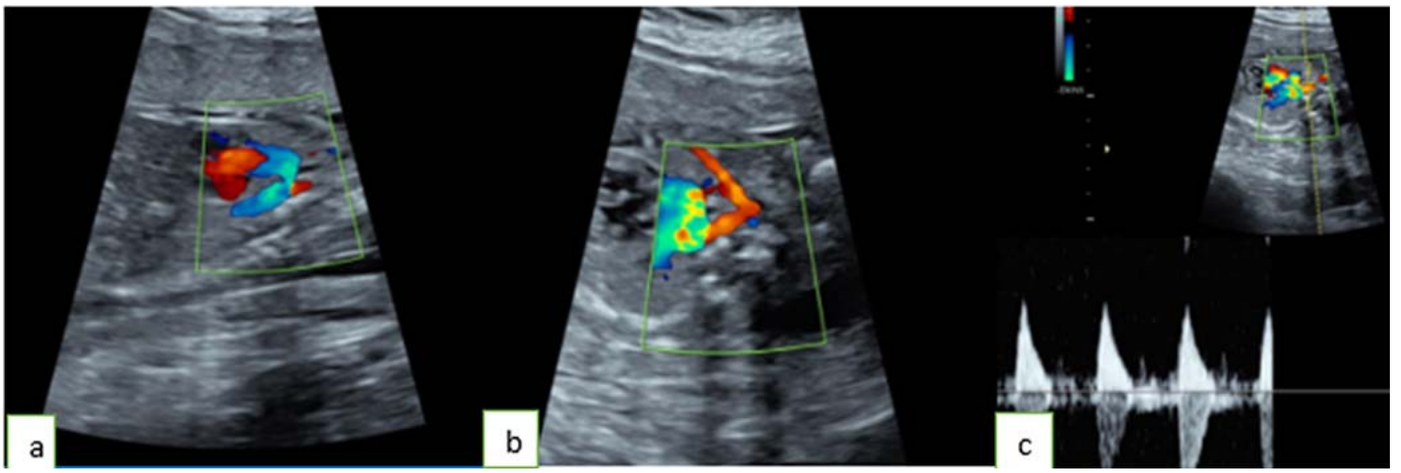

Figure 2: *Transabdominal color Doppler axial (a), semi-axial (b), and power Doppler image show an aberrant right subclavian artery. ARSA arises directly from the junction of the aortic arch and ductus arteriosus and passes behind the trachea to the opposite*

Statistical analyses were performed using SPSS version 22 (Statistical Package for the Social Sciences, Chicago). Data were expressed as mean ± standard deviation, median (range), and percentage. The mean gestational week of detection of ARSA, cardiac and extracardiac anomalies accompanying ARSA, and birth data of newborns were collected.

Since cell-free DNA testing was not performed in our center, we recommended amniocentesis for all pregnancies with ARSA in the fetus. Postnatal echocardiography was performed on all newborns by a fetal cardiologist. Genetic testing was applied to newborns with suspected fetal anomalies and whose mothers refused to perform amniocentesis during pregnancy.

Results

Our study included 6205 patients who underwent detailed ultrasonography in our clinic between January 2017 and June 2020. Our detailed ultrasonography application week was between 16-24 weeks. During this period, ARSA was detected in 47 of our patients. One of these was a false positive case that was not detected on postnatal examination. Therefore, 46 patients were included in this study. And, we detected 16 fetuses with Down syndrome in the same period.

One of them was a dichorionic diamniotic twin pregnancy and the others were singleton pregnancies.

The detection rate of ARSA in the normal population in our study was 0.7% (46/6205). While ARSA was the only ultrasonographic finding in 28 patients, extra anomalies were observed in 18 patients. Demographic data of patients and infants with ARSA are given in table I.

Down syndrome was detected in four fetuses, but all had extra anomalies except ARSA. Therefore, down syndrome was not detected in the isolated ARSA group. Cardiac findings (atrial and/or ventricular septal defect) were present in all patients diagnosed with Down syndrome genetically. In addition, all fetuses with Down syndrome had extracardiac anomalies. Ultrasonographic findings of a fetus with Down syndrome are shown in table II.

Atrioventricular (AV) septal defect was found in four of the nine patients in the group with the cardiac anomaly, and echogenic intracardiac focus (EIF) was found in the other four. In the group with cardiac and extracardiac anomalies accompanying ARSA, 5 patients' prenatal cardiac findings and 2 patients' postnatal cardiac findings were detected. Prenatal findings were the hyperechogenic focus in 4 patients and atrial septal defect in 1 patient. Extracardiac findings were detected in 8 patients. In 2 patients prenasal thickness increased, in 3 patients pyelectasis, in 2 patients increased nuchal fold thickness, and in 2 patients' choroid plexus cysts were detected. Abnormalities accompanying ARSA in patients with normal karyotype are shown in table III.

To our knowledge, none of the patients had dysphagia or dyspnea.

Table I: *Characteristics of the study group*

Maternal age (min-max)	30(21-41)
Number of fetuses with Down Syndrome*	4(%8)
Isolated ARSA	28(%60)
Cardiac anomalies*	8(%17)
Extracardiac anomalies*	14(%30)
Cardiac and extracardiac anomalies*	6(%13)
Termination	1
Mean gestational week at birth	37,93
Mean birth weight	3325,83
5 min APGAR score	7,9
10 min APGAR score	9,0
Female sex*	17(%36)
Mean head circumference	34,34
Amniocentesis*	14(%30)
Fetal height (min-max)	49,75(43-56)
Cesarean section rate	11(%23)

**: Number (percentage)*

Table II: *Ultrasonographic findings of the fetus with Down syndrome.*

Patient number	Maternal age (years)	Cardiac anomaly	Other anomalies	Outcome
1	36	VSD	Short femur and humerus, renal pyelectasis	Had surgery
2	33	AVSD	Polihydramnios, brachycephaly	Post partum ex
3	34	ASD	Prenasal thickness Low set-ears, flat face, clinodactyly, brachycephaly, increased nuchal fold thickness, polyhydramnios	Live
4	41	VSD	High risk of a combined test	Termination of pregnancy

VSD: Ventricular septal defect, AVSD: Atrioventricular septal defect, ASD: Atrial septal defect

Table III: *ARSA accompanying anomalies in patients with normal karyotype*

Patient number	Maternal age (years)	Cardiac anomaly	Other anomalies	Outcome
1	34	-	CPC, Piyelectasia	Normal
2	25	-	CPC	Normal
3	25	HEF	ALSA	Normal
4	38	-	Prenasal thickness	Normal
5	42	-	Polihydramnios	Normal
6	24	-	Placentomegaly	Normal
7	21	-	NF thickness, third-trimester oligohydramnios	Normal
8	35	HEF	NF thickness	Normal
9	34	-	IUGR	Normal
10	28	-	Third trimestr anhydramnios	Normal
11	33	-	Piyelectasia	Normal
12	33	ASD	-	Angiography
13	32	HEF	-	Normal
14	30	HEF	-	Normal

Discussion

Studies investigating the relationship between Down syndrome and ARSA have been made in the second trimester of pregnancy. Although the detection rate is low, there are studies in the literature that ARSA can be detected in the first trimester. Martinez-Payo et al. showed that the sensitivity and specificity of ARSA in first-trimester pregnancy were 68% and 99.9%, respectively (12). We think that BAS screening in the first trimester should be a part of suspected fetal anomalies. There is no evidence in the literature that an invasive procedure should be performed when isolated BSS is detected in the USG examination. Some fetal anomalies can only be detected in the second-trimester USG examination. That is, if we perform invasive procedures on all ABS detected in the first trimester, our invasive procedure rate will increase.

The detection rate of ARSA in the general population is 0.4-1.1%. In our study, the rate of ARSA was 0.7%, which is consistent with the literature (4,9,13). However, there are studies in the literature showing that a higher chromosomal abnormality can be detected than standard fetal chromosomal tests when chromosomal microarray analysis (CMA) is performed (14). We do not know the minor chromosomal anomaly rates in our population, since we could not perform CMA testing in our center.

In a series published in the literature, Trisomy 18 was found in 1 of 28 ARSA fetuses with ARSA (15). However, no trisomy 18 cases were detected in our group. In another series, chromosomal anomalies were found in 17.8% of 140 ARSA fetuses, and 11.4% of them were reported as Trisomy 21 (16). In our study, 8% (4/46) of the fetuses with ARSA were diagnosed with Down syndrome. All these cases had cardiac and extra-cardiac anomalies. In the first patient, only ventricular septal defect (VSD) was observed. The second one had increased prenasal thickness, low ear, flat face, regressed cystic hygroma, clinodactyly, brachycephaly, nuchal fold thickness, and polyhydramnios. The third had VSD, bilateral renal pyelectasis, and short extremity. VSD was detected in the ultrasonography of the fourth fetus and the first-trimester screening test was reported as high risk. We detected a cardiac anomaly in all patients with Down syndrome. If Down syndrome is suspected in a patient with ARSA detected in the prenatal period,

we think that cardiac anomaly findings should be present in these patients. If ARSA and other cardiac anomaly findings are found together in the USG examination during the prenatal period, a genetic analysis should be performed for Down syndrome.

There are different studies in the literature about the anomalies accompanying ARSA. Sucu et al. found single umbilical artery and nasal bone hypoplasia as the most common anomaly accompanying ARSA in their study (17). However, in our study, the most common cardiac anomaly accompanying ARSA was cardiac HEF.

We think that if genetic testing is to be done, single standard chromosome analysis should be done. Because in previous studies, it has been shown that no abnormal findings were detected in the chromosomal microarray analysis (18).

Conclusion

We did not find any chromosomal anomalies in any of the patients with isolated ARSA. Therefore, we do not recommend invasive intervention in patients with isolated ARSA. On the other hand, our study confirmed that ARSA screening should be a part of a detailed fetal ultrasonographic examination. Because, it depends on the person doing the prenatal sonographic examination, sometimes some abnormalities cannot be detected. On the contrary, we think that ARSA can be detected easily with color Doppler ultrasonography. Once we find ARSA, we can look for other anomalies that we couldn't detect in the previous inspection. Further studies with larger patient groups are needed.

Informed Consent: All patients gave written informed consent after they were informed about the study protocol and aim.
Availability of data and materials: The data supporting this study is available through the corresponding author upon reasonable request.
Conflict of Interest: No conflict of interest was declared by the authors.
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