



Diagnosis, Treatment and Follow-up of Fetal Cardiac Arrhythmia

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ABSTRACT

Aim: The importance of managing fetal arrhythmia has increased with advances in fetal echocardiography. We aimed to describe the incidence, types, clinical characteristics, treatments, and follow-ups of patients diagnosed with fetal arrhythmia in our center.

Materials and Methods: Fetal echocardiographic examinations performed in our units between January 2016 and September 2019 were retrospectively evaluated. Fetal arrhythmias and their subtypes were identified using M-mode and Doppler echocardiography in all patients. Maternal age, gestational age, history of maternal or gestational pathology, diagnoses, and medications were recorded. Fetal arrhythmias were categorized into three main groups: 1) Irregular heart rhythm (ectopic beats), 2) Bradycardias: a ventricular rate less than 110 bpm; and 3) Tachycardias: a ventricular rate exceeding 180 bpm.

Results: A total of 60 patients were diagnosed with fetal arrhythmia, corresponding to an overall incidence of 0.5%. The mean maternal and gestational age of those patients with fetal arrhythmia were 28.35±4.88 years and 31.03±5.94 weeks. One patient had maternal systemic disease, and four had concurrent congenital cardiac disease. Fetal tachycardia, bradycardia, and irregular heart rhythm were detected in 10 (16.6%), 8 (13.3%), and 42 (70%) patients, respectively.

Conclusion: Fetal echocardiography represents the main diagnostic tool for prenatal evaluation of fetal arrhythmias, which have a variable prognosis depending on the type of arrhythmia. The most common fetal arrhythmia, the irregular heart rhythm, generally does not necessitate any treatment and resolves spontaneously. The treatment plan in patients should be based on etiology and fetal conditions.

Keywords: Fetal echocardiography, fetal arrhythmia, tachycardia, bradycardia, irregular heart rhythm

Introduction

The development of fetal echocardiography has led to an increased awareness among clinicians regarding the importance of fetal arrhythmia management (1). Although most fetal arrhythmias are of benign nature, certain types of arrhythmias may be associated with certain adverse consequences such as fetal hydrops, cardiac dysfunction, and even fetal mortality (2). Therefore, fetal heart rate (FHR) should be evaluated carefully in all pregnancies.

The detection of normal fetal cardiac rhythm is based on the documentation of regular atrial and ventricular rhythm, with a normal rate for gestational age. Each atrial activity is followed by a ventricular activity within the framework of a normal atrio-ventricular (AV) time interval, corresponding to a normal AV conduction rate of 1:1 (3).

Currently, echocardiography represents the most widely used tool for diagnosis and follow-up of fetal arrhythmias in clinical practice. Although non-invasive techniques to record electrophysiological signals from the fetal heart have been

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developed and have proven valuable in gathering important information on the pathophysiology of arrhythmias, they are mainly used as research tools and only in a limited number of centers (4).

Perinatal management of fetal arrhythmia is important to improve the outcome of an affected fetus. Accurate prenatal diagnosis is crucial for the selection of appropriate prenatal and postnatal treatments. In this study, we aimed to describe the incidence, types, clinical characteristics, treatments, and follow-ups of those patients diagnosed with fetal arrhythmia in our center.

Materials and Methods

Fetal echocardiographic examinations performed in our secondary and tertiary healthcare units between January 2016 and September 2019 were retrospectively evaluated. Fetal arrhythmias and their subtypes were diagnosed with M-mode and Doppler echocardiography in all patients. Maternal age, gestational age, history of maternal or gestational pathology, diagnoses, and medications were recorded in those patients diagnosed with fetal arrhythmia. This study was approved by the University of Health Sciences Turkey, Tepecik Training and Research Hospital Clinical Researches Ethical Committee (no: 2020/11-66).

Initially, signs of structural cardiac abnormality or cardiac failure were investigated in all fetuses. In those diagnosed with fetal arrhythmia, the type of arrhythmia was ascertained using M-mode echocardiography and Doppler ultrasound. Simultaneous atrial and ventricular wall movements were examined via M-mode echocardiography, while the type of arrhythmia was determined using the mitral inflow and aortic outflow (mitral valve flow/aorta flow) technique via Doppler echocardiography.

Classification of Fetal Arrhythmias

Fetal arrhythmias were assessed in three main groups: 1) Irregular heart rhythm (ectopic beats); supraventricular premature beats and ventricular premature beats; 2) Bradyarrhythmias: ventricular rate less than 110 bpm (sinus bradycardia, 2:1 AV block, complete AV block), and 3) Tachyarrhythmias: Ventricular rate exceeding 180 bpm [sinus tachycardia, supraventricular tachycardia (SVT), ventricular tachycardia (VT)].

Statistical Analysis

We used the Statistical Package for Social Sciences (SPSS, version 23.0, SPSS Inc., Chicago, IL, USA). Descriptive analysis was used for demographic, clinical, and medication variables.

Results

Between January 2016 and September 2019, a total of 12,002 patients underwent fetal echocardiography. Among these, 60 were diagnosed with fetal arrhythmia. Clinical presentation included irregular rhythm in 42 patients, bradycardia in 8, and tachyarrhythmia in 10. These findings corresponded to a fetal arrhythmia incidence of 0.5% in the overall study population.

The mean maternal age in those patients with fetal arrhythmia was 28.35 ± 4.88 years (minimum: 19, maximum: 38 years), while the gestational age was 31.03 ± 5.94 weeks. One patient had maternal systemic disease, and 4 had concomitant congenital cardiac disorders. The demographic and clinical characteristics of patients with fetal arrhythmia are shown in Table I.

Ten patients, with an average maternal age of 29.2 ± 3.64 years and gestational age of 31.4 ± 6.36 weeks, had fetal tachycardia. All cases with fetal tachycardia had SVT. One patient with SVT had a cardiac anomaly consisting of a single ventricle defect and died in the first postnatal week after birth at 33 weeks of gestation.

Bradycardia was present in 8 patients, who had an average maternal age of 26.00 ± 4.40 years and gestational age of 27.7 ± 5.47 weeks. Dexamethasone treatment was started in one patient diagnosed at 29 weeks of gestation who had maternal antibody positivity. This patient was born at 38 weeks of gestation, with a heart rate between

Table I. Demographic and clinical characteristics in patients with fetal arrhythmia

	n=60
Gestational age (weeks) (mean \pm SD)	31.03 \pm 5.94
Maternal ages (years) (mean \pm SD)	28.35 \pm 4.88
Congenital heart disease n (%)	4 (6.6)
Maternal disease n (%)	1 (1.6)
Mortality n (%)	3 (5)
Fetal tachycardia n (%)	10 (16)
Maternal ages (years)	29.2 \pm 3.64
Gestational age (weeks)	31.4 \pm 6.36
Fetal bradycardia n (%)	8 (13.3)
Maternal ages (years)	26.00 \pm 4.40
Gestational age (weeks)	27.7 \pm 5.47
Irregular cardiac rhythm n (%)	42 (70)
Maternal ages (years)	28.28 \pm 5.23
Gestational age (weeks)	32.09 \pm 5.15
SD: Standard deviation	

80 and 90 bpm. Another patient with left atrial isomerism and AV septal defect (AVSD) was diagnosed at 23 weeks of gestation. Although salbutamol was started, this was followed by a subsequent termination of the pregnancy. A further patient with AV block had a heart rate between 60 and 70 bpm, and was only followed up due to the absence of signs of hydrops. 4 other patients had sinus bradycardia, with a heart rate greater than 60 bpm, and these patients did not receive any medical treatment due to an absence of the signs of heart failure or hydrops. Additionally, no signs of cardiac failure were observed during their follow-up period.

Forty-two patients were found to have irregular heart rhythm. The mean maternal and gestational ages in these patients were 28.28 ± 5.23 years and 32.09 ± 5.15 weeks, respectively. Among these, only one patient had diaphragmatic herniation and supraventricular premature beats coexisting with dextrocardia. In the remaining cases, no cardiac pathology was found. The patient with diaphragmatic herniation died at postnatal 24 hours. The irregular heart rhythms were normalized in the remaining group.

Thus, the majority of our patients diagnosed with fetal arrhythmia had irregular cardiac rhythm (70%), followed by SVT (16.6%), and bradycardia (13.3%). Their echocardiographic results, clinical findings, and outcomes of arrhythmia are shown in Table II.

Discussion

Fetal arrhythmias occur in a small percentage (0.6-2.0%) of all pregnancies (5,6), and the frequency of pediatric cardiologic referral of these patients is reported to be between 10% and 20% (7). Incidence rates have not been provided in some previous studies due to the admission of patients specifically diagnosed with fetal arrhythmia to tertiary referral centers (8). However, we chose to present such data since patients from a secondary healthcare facility were also included in the sample population, in addition to a tertiary center. Thus, based on our results, the incidence of fetal arrhythmia was in the order of 0.5%.

Fetal Tachycardia

Tachycardia is generally defined as the presence of sustained FHR exceeding 180 bpm. The detection of a fast heart rate greater than 180 bpm in a fetus constitutes a medical emergency since it may lead to fetal hydrops or premature delivery as well as increased perinatal morbidity and mortality. Sustained tachycardia with high ventricular rate in the early gestational weeks is more likely to be

associated hydrops with fetalis. In the current study, two patients had signs of hydrops fetalis due to SVT occurring at 22 and 25 weeks of gestation.

The causes of fetal tachycardia include sinus tachycardia, re-entrant SVT, atrial flutter, atrial ectopic tachycardia, junctional ectopic tachycardia, and VT. Among these, re-entrant SVT represents the most common type of fetal tachycardia (9), comprising almost two-thirds of all cases with this condition (5). Re-entrant tachycardia mostly occurs between 24 and 32 weeks of gestation. Eight of our patients with a mean gestational age of 31.4 ± 6.36 weeks had re-entrant tachycardia. The second most common type of tachycardia was AF, which was detected in two cases. Conversely, junctional ectopic tachycardia and VT are uncommon and were not identified in any of our patients. Approximately 2% of those patients with fetal tachycardia have been reported to have coexisting congenital cardiac disorders (10,11). In another study, 15% to 18% of fetuses with fetal arrhythmia were also found to have concomitant congenital cardiac abnormalities (12). In our study, congenital cardiac disorder was present in 12.5% of those patients with SVT and in 6.6% of those with fetal arrhythmia.

In one study involving 29 cases diagnosed with fetal arrhythmia, the subtypes were fetal tachycardia, fetal bradycardia, and irregular heart rhythm in 41.4%, 17.2%, and 41.4% of the cases respectively (13). In the current study 16.6% of those patients with fetal arrhythmia had fetal tachycardia, and the most common type was irregular heart rhythm.

Currently, there is no consensus regarding the first agent of choice for the treatment of re-entrant SVT, and the decision should be based on the condition of the fetus. For a non-hydropic fetus, the commonly used drugs are sotalol, flecainide, and digoxin, while flecainide and sotalol have been shown to be readily transferred through the placenta and therefore may be used for hydropic fetuses (14). In a study by Jaeggi et al. (15), flecainide was found to be slightly more effective than sotalol in hydropic fetuses. When no response is obtained with single-agent therapy, combinations may be tried, such as amiodarone/digoxin, amiodarone/flecainide, sotalol/digoxin, and sotalol/flecainide on the basis of studies reporting their benefits (15,16). Arrhythmia was terminated with digoxin in all of our patients with re-entrant SVT.

Currently, digoxin and sotalol are used to treat AF, with sotalol preferred in the presence of hydrops. Of our two cases with AF, one responded to digoxin, while the other was followed up with digoxin/sotalol combination therapy.

Table II. Echocardiographic results, clinical findings, and outcome of arrhythmia by subtype

Fetal arrhythmia type	Incidence	Echocardiographic findings	Clinical findings	Treatment	Outcome
Tachycardia	0.08%				
Case 1 (week 25)		Hydrops fetalis	Atrial flutter	Digoxin Sotalol	Birth: 36 th week recurrent episodes of SVT in postnatal period Cured with propranolol
Case 2 (week 22)		Hydrops fetalis	Re-entrant SVT	Digoxin Sotalol	Birth: 34 week SVT disappeared in postnatal period
Case 3		Single ventricle defect	Atrial flutter	Digoxin	Recurrent episodes of SVT and patients died
Case (4,5,6,7,8,9,10)		Normal	Re-entrant SVT	Digoxin	SVT disappeared
Bradycardia	0.06%				
Case 1		Left atrial isomerism - AVSD	cAV block bradycardia	Salbutamol	Patient died in fetal period
Case 2		Normal	cAV block bradycardia	-	Followed in postnatal period
Case 3		Maternal Anti-Ro + Normal	cAV block bradycardia	Dexamethasone	Cured with dexamethasone
Case 4		Aortic arch hypoplasia	Bradycardia	-	Bradycardia disappeared in postnatal period
Case (5,6,7,8)		Normal	Sinus bradycardia	-	Postnatal normal
Irregular heart rhythm	0.34%			-	
Case 1		Dextrocardia, diaaphragmatic hernia	Ectopic beats	-	Patient died in postnatal period
Case 2-42		Normal	Ectopic beats	-	Normal

SVT: Supraventricular tachycardia, cAV: Complete atrioventricular, AVSD: Atrio-ventricular septal defect

However, this latter patient died at postnatal week 1 due to a coexisting cardiac anomaly.

Fetal Bradyarrhythmia

Fetal bradycardia is defined as a regular heart rate below 100-110 bpm without taking the gestational age of the fetus into consideration (6). It may be caused by sinus bradycardia, premature atrial contractions (PAC) with block, or AV block. Transient bradycardia, generally occurring during the second trimester, is benign and does not require treatment (14).

Persistent fetal bradycardia is relatively rare. Slow heart rate may develop due to a congenital or acquired injury in the sinoatrial node. Possible causes include viral myocarditis, inflammation and fibrosis due to collagen tissue disorders, maternal treatment with β blockers and sedatives, fetal distress, hypoxia or acidosis. Additionally, in patients with persistent sinus bradycardia, long-QT syndrome should be investigated during the postnatal period. According to Mitchell et al. (17), 40% of long QT syndrome cases evaluated by fetal magnetocardiography were referred due to sinus bradycardia.

Nearly 50% of cases with complete AV block are associated with complex cardiac malformations (18) (left atrial isomerism, AV septal defect, corrected transposition of the great arteries) or maternal autoantibodies (associated with autoimmune diseases such as systemic lupus erythematosus) (19).

Of the three patients with complete AV block in our study, two had coexisting anomalies (one had left atrial isomerism and AVSD, and one had maternal anti-Ro antibody positivity). In this regard, it should be remembered that the combination of complete AV block and major structural heart disease carries high mortality. When hydrops is present, the mortality rate approaches 100% (5). In this study, the pregnancy associated with fetal left atrial isomerism was terminated.

Treatment of fetal bradycardia depends on the etiology, ventricular rate, and presence or absence of cardiac failure. If the FHR is less than 55 to 60 bpm, beta-mimetics (terbutaline, salbutamol, isoprenaline) may be tried as a first line therapy (14,20). These agents may increase the

fetal ventricular rate by around 10-20% and reverse hydrops as well (21). Immune-mediated AV block may benefit from in utero treatment with fluorinated steroids, intravenous immunoglobulin, or both. Dexamethasone is believed to reduce inflammation (22). Although no consensus exists, many clinicians administer dexamethasone 4 to 8 mg/d to treat second degree AV block, recent onset AV block, or severe cardiac dysfunction and hydrops. In our study, salbutamol treatment was given during the fetal period in the patient with atrial isomerism-AVSD, while the other patient with maternal antibody positivity benefited from dexamethasone.

Irregular Cardiac Rhythm

Irregular heart rhythm, also called premature beat, premature contraction, ectopic beat or extra-systole, can originate from the atria, the AV junction, or the ventricle, and bypasses the sinus node. Irregular heart rhythms are the most common abnormal rhythms seen in clinical practice.

Fetal ectopy occurs in up to 1 to 2% of all pregnancies and has been reported to be a relatively benign condition (5). In a study by Capuruço et al. (23), fetal ectopic beats were the most common type of fetal arrhythmia with an incidence of 55.5%. Similarly, this was also the most common fetal arrhythmia, occurring in 70% of our patients. In our study, 0.34% of all pregnancies were associated with irregular heart rhythm. Most irregular beats originate from the atrium (PAC), with premature ventricular contractions (PVC) being much less frequent than PAC, with an estimated prevalence ratio of 10:1 for PAC vs. PVC (24). In clinical practice, ectopic beats are mostly detected in the third trimester of pregnancy (7). Similarly, in this study, the mean gestational age of patients with irregular heart rhythm was 32.09 weeks.

The majority of fetuses evaluated for irregular rhythm have a structurally normal heart. In a recent study of 256 singleton fetuses with an irregular heart rhythm, only two (0.8%) had a congenital heart malformation (25). In our study, only one patient among 42 cases (2.3%) had a coexisting cardiac anomaly. In another report describing 306 fetuses with irregular rhythm, isolated extrasystoles were diagnosed in 298 and were still present in 10 (3.4%) at delivery (26). Among our patient group, 1 (2.3%) had extra-systoles that persisted for up to 3 days following delivery. In patients with fetal ectopic beats, the risk of developing fetal tachycardia is estimated to be between 0.5% and 1%. The presence of couplets and blocked atrial bigeminy increases this risk to approximately 10%. Fetal ectopic beats are

generally of benign nature, most resolving spontaneously. No medical treatment is considered necessary for these patients although it is recommended that these patients should be assessed on a weekly basis with respect to SVT and VT (14).

Study Limitations

The absence of long-term follow-up findings in the postnatal period can be assessed as a limitation of our study.

Conclusion

Fetal echocardiography represents the main diagnostic tool for prenatal evaluation of fetal arrhythmias. In all patients with suspected tachyarrhythmia or bradyarrhythmia, a fetal echocardiography should be performed to evaluate cardiac structures and functions. Fetal arrhythmias may present with variable types and prognostic consequences, with no direct effects on fetal growth and development. The etiology and fetal conditions are the main determinants of the management strategy for fetal tachyarrhythmias and bradyarrhythmias.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Tepecik Training and Research Hospital Clinical Researches Ethical Committee (no: 2020/11-66).

Informed Consent: Informed consent was not obtained because this was a retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: A.Ş., T.D., Data Collection or Processing: T.D., Analysis or Interpretation: A.Ş., T.D., Literature Search: A.Ş., T.D., Writing: A.Ş.

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