Atrioventricular and ventricular septal defects; topographical analysis and impact of associated cardiac and extracardiac findings and postpartum outcome

Atrioventriküler ve ventriküler septal defektler; topografik değerlendirme ve ek kalp ve kalp dışı bulguların etkisi ile doğum sonrası sonuçları

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Abstract

Objective: The aim of this study was to evaluate prognosis of types of ventricular septal defects and coexistence of associated cardiac and extracardiac defects.

Methods: 120 prenatal diagnosed pregnancies associated with ventricular septal pathology were retrospectively evaluated and divided into four groups, as atrioventricular septal defects, perimembranous septal defects, muscular septal defects and univentricular formation. Each group was divided further into four groups, as isolated defect, co-existing extracardiac defect, septal defect with extracardiac defect and septal defect with co-existing cardiac and extracardiac defect. Postnatal follow-up was continued at least until 8 months of life.

Results: Median gestational age at diagnosis was 26.3 weeks, 47 cases were diagnosed before 24 weeks. After dispersion of septal defects there was a statistical significance of p=0.0089 between groups. Of 31 cases with atrioventricular septal defects, only one case survived (3.2%) and there was a high association with extracardiac defects and abnormal karyotype (p=0.002). 69 cases with perimembranous ventricular septal defects were diagnosed, and 24 cases (34.8%) survived with significance for abnormal karyotype (p=0.039). Of 18 cases born with muscular septal defects 12 cases (66.7%) stay alive. We had two cases with univentricular structure; both cases decided for termination of pregnancy.

Conclusion: The more complicated and severe the pathology, the worse the prognosis. Individualized counseling is the most important point in decision making together with families.

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Key words: Atrioventricular septal defects, perimembranous ventricular septal defects, muscular ventricular septal defects, associated abnormalities, prognosis

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Özet

Amaç: Bu çalışmamızın amacı venriküler septumdaki defektleri ve eşlik eden ek kardiyak ve kalp dışı defektlerin prognoz üzerine etkisini değerlendirmektir.

Yöntemler: Prenatal dönemde tanı almış 120 ventriküler septal patoloji olgusu, retrospektif olarak, atriovenriküler septal defekt, perimembranöz septal, müsküler septal defekt ve tek ventrikül oluşumu olarak 4 ayrı grup içinde değerlendirilmiştir. Her bir grup daha sonra tekrar izole defektler, eşlik eden kalp dışı defektler, eşlik eden kalp defektleri ve eşlik eden kalp ve kalp dışı defektleri olmak tekrar 4 grup içinde değerlendirildi. Olgular doğum sonrası süreçte en az 8 aylık oluncaya kadar izlendi.

Bulgular: Prenatal tanı sırasında ortalama gebelik haftası 26.3 olup, 47 olgu 24. gebelik haftasından önce tanı almıştır. Septal defektlerin dağılımından sonra gruplar arasında istatistiksel olarak anlamlılık saptanmıştır (p=0.0089). 31 atrioventriküler septal defekt olgusunun sadece 1 tanesi (%3.2) hayatta kalmış olup, bu grupta kalp dışı defektler ve anormal karyotip ilişkisi yüksek olarak saptanmıştır (p=0.002). 69 perimembranöz ventriküler septal defekt olgusunun 24 tanesi (%34.8) hayatta kalmış ve anlamlı anormal karyotip ilişkisi saptanmıştır (p=0.039). 18 müsküler septal defekt olgusunun 12 tanesi (%66.7) hayatta kalmıştır. Olgularımızn içinde iki univentriküler ventrikül oluşumu olgusu, gebeliğin sonlandırılmasını istemiştir.

Sonuç: Olgulardaki komplike ve patolojik ciddiyet arttıkça, prognoz kötüleşmiştir. Aileler ile yapılan danışmanlıkta, olguların kişiselleştirilerek verilmesi ve buna uygun karar verilmesi uygundur.

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Anahtar kelimeler: Atrioventriküler septal defekt, perimembranöz ventriküler septal defekt, müsküler ventriküler septal defekt, eşlik eden anomaliler, prognoz

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Introduction

Congenital heart disease (CHD) is the most frequent congenital disorder and has significant pre- and post-natal morbidity and mortality (1). CHDs are believed to be multifactorial disorders arising from the combined effect of genetic predisposition and environmental factors (2). Ventricular septal defects (VSDs) are the most frequent congenital cardiac anomalies (3-5). The incidence of VSDs ranges from 3-56/1000 live births (3), depending on the screening method. Anatomically, VSDs are divided into defects of the membranous or muscular part of the interventricular cardiac septum. The etiology of VSDs is still uncertain. It is expected that in 4% of cases, a chromosomal or genetic defect exists (3, 6-8).

Atrioventricular septal defects (AVSDs) are a group of anomalies that share a defect of the atrioventricular septum and abnormalities of the atrioventricular valves. AVSDs are divided into partial and complete forms. In partial AVSDs, a primum atrial septal defect (ASD) is always present and there are two distinct mitral and tricuspid valve annuli. The complete form of AVSDs also includes a primum ASD, but it is contiguous with an inlet ventricular septal defect (VSD), and the common atrioventricular valve has a single annulus (9). The estimated incidence of AVSDs ranges from 24-31/100,000 (10) live births. There is a strong association between AVSDs and Down's syndrome; one-half of patients with AVSDs having Down's syndrome (11).

The objective of this study was to portray the characteristics and outcome of prenatally detected peri-membranous VSDs, muscular VSDs, and AVSDs, depending on the associated cardiac and extracardiac abnormalities and their effect on aneuploidy and the outcome of fetuses, after a 1-year follow-up.

Material and Methods

Between January 2002 and December 2007, 8953 pregnancies were screened using fetal echocardiography and genetic sonogram, and 155 cases with CHD were detected in our Perinatology Unit. When a heart defect is diagnosed or suspected, one of our four physicians at the center performs a detailed anatomic assessment, in most cases in the presence of a pediatric cardiologist. For optimal fetal heart screening, the five short-axis views (12) are used for the examination, including the sagittal view of the aortic and ductal arches, if needed. This was a retrospective study with 120 cases of fetuses with peri-membranous and muscular VSDs and AVSDs as a component of other CHDs, associated with other extracardiac congenital abnormalities or as isolated findings. CHDs without a septal defect were excluded from the study. Partial and complete forms of AVSDs were counted together. All cases were diagnosed prenatally and counseled about clinical outcomes and follow-up.

Every group of VSDs was subdivided into the four subgroups as (a) isolated cardiac findings, (b) septal defects with co-existing cardiac findings, (c) septal defects with extra-cardiac defects, and (d) septal defects with co-existing cardiac and extracardiac findings.

The study was closed to new follow-up data on 1 January 2008, but the follow-up period for survivors was calculated to the last follow-up available, rather than the closing date of the study.

The following information was retrieved for all cases from our computerized database: gestational age at diagnosis, presence of other cardiac defects, presence of extracardiac defects and chromosomal anomalies, location of the defect, Doppler demonstration of a flow defect, pregnancy outcome, and neonatal follow-up. The location of the defect was categorized as an ASD, peri-membranous septal defect, muscular septal defect, or univentricular formation.

Fetal karyotypes were available in 108 cases (90.0%), except for 6 cases with isolated muscular VSDs. When genetic abnormalities were suspected in the neonatal period, postnatal karyotyping was also offered to the parents.

After completion of the fetal anomaly work-up, including cardiac and extracardiac abnormalities, a multidisciplinary medical panel consisting of perinatologists, pediatricians, and pediatric surgeons counseled the couple. Our hospital's Ethical Committee and Perinatal - Neonatal Council offered patients an opportunity to discuss prenatal findings, neonatal prognosis, and pregnancy management and options, including termination of pregnancy (TOP). Our hospital's Ethical Committee, Perinatal-Neonatal Council, and Institutional Review Board approved the follow-up and clinical management.

All neonates who survived the 2nd day of life and all fetuses that died after birth due to associated cardiac, extracardiac, or chromosomal anomalies were examined by our pediatric cardiologist. All surviving neonates were followed directly until 12 months of age. In the case of cardiac surgery, they were referred to three other cardiac surgery centers in Istanbul, but follow-up after surgery was continued in our center. Necropsies of all fetuses undergoing TOP were performed by our pathologists.

The GraphPad Prisma V.3 package program was used for statistical analyses in this study. In the data evaluation, descriptive statistical methods (mean and standard deviation) were used. Chi-square (χ^2) and Fisher's exact tests were used for qualitative data determination. The results were evaluated with a confidence level of 95%, and a significance level of $P < 0.05$.

Results

A final prenatal diagnosis of septal defects was made in 120 of 8953 cases referred to our Prenatal Diagnosis Unit. Thirty-one (25.8%) fetuses had AVSDs, 69 (57.5%) cases had peri-membranous VSDs, 18 (15.0%) fetuses had muscular VSDs, and 2 cases (1.7%) had univentricular heart formations. Of these 120 cases with septal defects, 6 cases with a prenatal diagnosis and normal karyotype findings were lost to follow-up after birth in the neonatal period and were excluded.

The mean gestational age at diagnosis was 24.3 weeks (range, 14-39 weeks). The mean maternal age at diagnosis was 27.0 years (range, 17-42 years). The indications for fetal echocardiography were as follows: suspected extracardiac malformations in 31 cases (25.8%), suspected CHD in 29 cases (24.1%), maternal diabetes in 3 cases (2.5%), growth restriction in 8

cases (6.7%), routine scan in 28 cases (23.3%), sibling history of CHD in 5 cases (4.2%), sibling history of extracardiac defects in 8 cases (6.7%), and other indications in 8 cases (6.7%).
Fetal karyotyping was performed in 108 cases, of which 22 (20.4%) had aneuploidies, as follows: 1 case (0.9%) of trisomy 13, 8 cases (7.4%) trisomy 18, and 12 cases (11.1%) of trisomy 21.

The dispersion of septal defects and associated cardiac and extracardiac findings in the described subdivided groups, aneuploidy findings, clinical outcomes of each group, and live cases after a 1-year follow-up are shown in Table 1. Thirty-seven cases (32.5% of 114 cases with a 1-year follow-up) survived with statistical significance between all 3 groups (AVSD, peri-

Table 1. Dispersion and outcome of cases (n=120)

Type of defect (n)	Outcome	Isolated	Coexisting cardiac	Extra-cardiac	Coexisting Cardiac + extra-cardiac
Alive at follow-up (%)					
AVSD (n=31)		1	10	6	14
	Alive birth	1	6	0	4
	TOP: a- aneuploidy	-	-	6 (5xT21, 1xT18)	5 (4xT21, 1xT18)
	b- other	-	3	-	5
	IUDF	-	1	-	-
	Postpartum death	1	5	-	4
Survivor: 1 (3.2%)	Alive (%)	0 (0%)	1 (10%)	0 (0%)	0 (0%)
	Aneuploidy (%)	-	-	100%	35.7%
Perimembranous VSD (n=69)		12	26 (29, but 3 cases lost in follow-up)	13	13 (15, but 2 cases lost in follow-up)
(five cases lost in follow-up)	Alive birth	10	19	4	7
	TOP: a- aneuploidy	1 (1xT21)	2 (1xT21, 1xT18)	5 (1xT21, 3xT18, 1xT13)	3 (1xT21, 2xT18)
	b- other	-	4	3	2
	IUDF	1	1	1	1
	Postpartum death	-	11	3	4
Survivor: 24 (34.8%)	Alive (%)	10 (83.3%)	8 (27.6%)	1 (7.7%)	3 (20.0%)
	Aneuploidy (%)	8.3%	6.9%	38.5%	20.0%
Muscular VSD (n=18)		6	3 (4, but 1 case lost in follow-up)	6	2
(one case lost in follow-up)	Alive	6	3	4	-
	TOP: a- aneuploidy	-	-	-	-
	b- other	-	-	2	1
	IUDF	-	-	-	1
	Postpartum death	-	-	1	-
Survivor: 12 (66.7%)	Alive (%)	6 (100%)	3 (100%)	3 (50%)	0 (0%)
	Aneuploidy (%)	-	-	-	-
Univentricular (n=2)			1		1
	Alive Birth		-		-
	TOP: a- aneuploidy		-		-
	b- other		1		1
	IUDF		-		-
Survivor: - (%0.0)	Alive (%)		0 (0%)		0 (0%)
	Aneuploidy (%)		-		-

AVSD: Atrioventricular septal defect; IUDF: intrauterine demise / death of fetus; T13: trisomy 13; T18: trisomy 18; T21: trisomy 21; TOP: termination of pregnancy; VSD: ventricular septal defect

membranous VSD, and muscular VSD) related to an abnormality (Table 2; χ^2=17.09; P=0.0089).

AVSD outcome

There was only one isolated case (3.2%) of AVSD, 10 cases (32.3%) with other co-existing cardiac defects, 6 cases (19.3%) with additional extracardiac defects, and 14 cases (45.2%) with cardiac- and extracardiac-associated defects. The survival rate was very poor with only 1 survivor (3.2%) in this group with AVSD associated with tricuspid atresia, hypoplastic right ventricle, and dilated left heart after surgery and a regular 1-year follow up.

Cases with additional extracardiac defects were more often related to aneuploidies, which were seen in this group of AVSD cases with additional extracardiac defects with 100% involvement and AVSD cases related with cardiac and extracardiac defects with 35.7% involvement. No relationship was found in the other subgroups with isolated and additional cardiac findings.

Postpartum deaths were more related with complex cardiac defects, probably depending on severe postpartum neonatal circumstances and complications in pediatric cardiac surgery.

Peri-membranous VSD outcome

The database included 69 cases with peri-membranous VSDs, of whom 12 (18.8%) were isolated, 26 (40.6%) had co-existing cardiac defects, 13 (20.3%) had extracardiac pathologies, and 13 (20.3%) were diagnosed with cardiac and extracardiac defects. Five cases were diagnosed during pregnancy, but lost during postnatal follow-up.

The survival rate was 34.8%, although 20 cases (29.0%) had a TOP and 4 cases (5.8%) involved an intrauterine death of the fetus (IUDF). The survival rate was highest in the isolated group (83.3%), although 1 case had trisomy 21 and 1 case had an IUDF. Postpartum death was especially noticeable in complex, co-existing cardiac defects with 15 cases (21.7%).

Aneuploidies occurred in all groups, but were especially manifest in extracardiac defects (8.3%, 6.9%, 27.6%, and 20.0% for all subgroups, respectively).

Muscular VSD outcome

Cases with muscular VSD constituted 15.0% of our database (18 cases). None of these pregnancies had chromosomal pathologies; the survival rate was highest in the group, with 66.7%.

All six cases with isolated muscular VSD survived after a 1-year follow-up with spontaneous closure of muscular VSDs in 4 cases. The prognosis of muscular VSDs with cardiac defects was good, with 3 live cases after birth and regular follow-up and 1 case lost after birth during the follow-up period.

The main reason of loss in this group was the decision for TOP in 3 cases, 1 case with IUDF, and 1 postpartum death.

We diagnosed 2 cases with univentricular cardiac formation with decisions for TOP in both cases.

Among extracardiac anomalies, central nervous system anomalies were the most common group, followed by the musculoskeletal system, gastrointestinal system, and genitourinary system anomalies (Table 3).

There was a significant statistical correlation between the site of the defect, findings of extracardiac defects, and fetal karyotype in AVSDs and peri-membranous VSDs (Table 4). The relative risk for aneuploidy in association with extracardiac defects was remarkable, with 2.2 AVSDs and 2.14 peri-membranous VSDs. The relative risk for aneuploidy with respect to extracardiac defects was similar in both groups.

Prenatal ultrasound findings with associated cardiac and extracardiac findings of aneuploid fetuses are given in Table 5.

A major influence on overall outcome was the proportion of parents opting for TOP (n=39, 32.5% of all cases). Termination was offered only in aneuploidy cases and severe cardiac abnormalities such as severe hypoplastic left or right heart, interruption of arcus aorta, mitral or tricuspid atresias causing chamber disproportion and / or defects and aortic and pulmonic hypoplasias causing severe outflow defects. All cases with aneuploidy (n=22), 12 cases related with severe cardiac pathology, and 5 cases associated with extracardiac abnormalities accepted TOP.

Twelve of 37 surviving cases were operated without postoperative complications. In 8 of 25 cases, spontaneous closure of septal defects was noted. Three cases had a pre- and post-natal diagnosis of isolated peri-membranous VSD and 4 cases had a diagnosis of isolated muscular VSD, in which one closure was seen in the intrauterine period. One case with a muscular VSD and omphalocele (operated because of anterior wall defect) also had spontaneous closure of the septum. Follow-up continues in 17 cases.

Table 2. Statistical findings of septal defects related to abnormality

	Diagnosed (n)	Alive (n, %)	Isolated (n, %)		Coexisting Cardiac (n, %)		Extracardiac (n, %)		Coexisting + Extracardiac (n, %)	
AVSD	31	1 (3.2%)	1	3.23%	10	32.26%	6	19.35%	14	45.16%
Perimembranous VSD	69	24 (34.8%)	12	17.39%	26	37.68%	13	18.84%	13	18.84%
Muscular VSD	18	12 (66.7%)	6	33.33%	3	16.67%	6	33.33%	2	11.11%

χ^2:17.09; p=0.0089

AVSD: atrioventricular septal defect; VSD: ventricular septal defect

Table 3. System specific and individual anomalies with septal defects

Anomalies	AVSD (n=31)*	Perimembranous VSD (n=69)*	Muscular VSD (n=18)*
Cardiovascular system	37	77	8
- Outflow tract anomalies	13	36	3
- Chamber disproportion	5	14	2
- Arrhythmias	2	-	1
- Isomerism	5	1	-
- Single umbilical artery	4	3	-
Musculoskeletal system	5	11	1
- Short limbs	1	1	-
- Polydactyly	3	3	1
- Talipes equinovarus	-	2	-
- Rockerbottom foot	1	2	-
Central nervous system	14	20	3
- Posterior fossa anomaly	-	6	1
- Ventriculomegaly	2	8	-
- Spine pathology	1	4	-
- Major findings (holoprosencephaly, corpus callosum agenesis etc.)	3	-	2
- Minor findings (choroid plexus cysts, nuchal fold etc.)	6	2	-
Genitourinary system	7	6	3
- Multicystic dysplastic kidney	1	1	1
- Pelvicaliectasis/hydronephrosis	5	4	1
Gastrointestinal system	6	8	5
- Omphalocele/gastroschisis	-	2	2
- Obstruction/duplication	2	4	2
- Echogenic intestines	3	1	1
Face, eye and neck	4	5	2
- cystic hygroma	2	2	1
- cleft lip/palate	1	3	-
Respiratory system	2	-	-

*A case can have more than one anomaly and hence the number of anomalies will exceed the total number

Table 4. Statistical findings of septal defect to chromosomal pathology /aneuploidy

		Isolated and/or coexisting cardiac defect (without extracardiac finding)		Extracardiac Findings (with isolated and/or coexisting cardiac findings)		P	RR
AVSD	Normal karyotype (n / %)	11	100.00%	9	45.00%	0.002	2.2 (1.36-3.60)
	Abnormal karyotype (n / %)	0	0.00%	11	55.00%		
Perimembranous VSD	Normal karyotype (n / %)	35	92.11%	18	69.23%	0.039	2.14 (1.27-3.60)
	Abnormal karyotype (n / %)	3	7.89%	8	30.77%		

AVSD: atrioventricular septal defect; VSD: ventricular septal defect

Table 5. Associated cardiac and extracardiac findings in aneuploidy cases

Karyotype	Gestational age at diagnosis (weeks)	Cardiac Findings	Extracardiac Findings
Trisomy 18	22	AVSD Double outlet right ventricle	Strawberry shaped head Micrognathia
Trisomy 18	18	AVSD	Strawberry shaped head Congenital diaphragmatic hernia Clenched hands
Trisomy 21	21	AVSD Single AV valve	Choroid plexus cyst Enlarged nuchal fold Hydronephrosis
Trisomy 21	19	AVSD	Ventriculomegaly Corpus callosum agenesis Hydrops fetalis Echogenic bowel
Trisomy 21	17	AVSD Single AV valve Tetralogy of Fallot	Enlarged nuchal Fold Hydronephrosis Skeletal dysplasia
Trisomy 21	19	AVSD	Enlarged nuchal Fold Echogenic bowel Hydronephrosis
Trisomy 21	16	AVSD Single AV valve	Enlarged nuchal Fold
Trisomy 21	24	AVSD	Choroid plexus cyst Hydronephrosis
Trisomy 21	22	AVSD	Multicystic dysplastic kidney Ambiguous genitalia
Trisomy 21	22	AVSD Tricuspid regurgitation	Gastrointestinal obstruction Single umbilical artery Polyhydroamnios
Trisomy 21	22	AVSD	Hydronephrosis Ventriculomegaly
Trisomy 13	24	Perimembranous VSD	Hypoplastic Vermis Facial cleft Polydactyly
Trisomy 18	27	Perimembranous VSD	Strawberry shaped head Hypoplastic Vermis Gastrointestinal obstruction Hydronephrosis Ambiguous genitalia Polyhydroamnios
Trisomy 18	15	Perimembranous VSD	Cystic hygroma
Trisomy 18	26	Perimembranous VSD Double outlet right ventricle Tricuspid atresia Aort stenosis	Hypoplastic Vermis Intrauterine growth retardation
Trisomy 18	27	Perimembranous VSD Double outlet right ventricle Aort stenosis	Dandy Walker variant
Trisomy 18	18	Perimembranous VSD	Choroid plexus cyst Rockerbottom foot

Trisomy 18	26	Perimembranous VSD Tetralogy of Fallot Pulmonary stenosis	none
Trisomy 21	24	Perimembranous VSD Double outlet right ventricle Pulmonary stenosis	none
Trisomy 21	18	Perimembranous VSD	Hydronephrosis
Trisomy 21	22	Perimembranous VSD	none
Trisomy 21	14	Perimembranous VSD Hypoplastic left heart Hypoplastic arcus aorta	Ventriculomegaly Neural tube defect Intrauterine growth retardation

AV: atrio-ventricular; AVSD: atrioventricular septal defect; VSD: ventricular septal defect

Discussion

Atrioventricular, peri-membranous, and muscular septal defects are important congenital cardiac abnormalities which can be diagnosed prenatally with significant accuracy. Fetuses with septal defects constitute a heterogeneous group which differ in their prognoses in association with additional cardiac and extracardiac defects. Those cases diagnosed prenatally are likely to be biased in favor of features that more readily bring them to the awareness of the ultrasonographer (10). The diagnosis of AVSD in a fetus should initiate not only a detailed examination of the rest of the heart, but also of the entire fetus. Even when the fetal karyotype and detailed ultrasound anomaly scan are apparently normal, important anomalies and genetic syndromes may become apparent after birth, and parents must be counseled with this in mind (10).

The embryologic development of AVSD and VSD differ. The normal embryogenesis of the atrioventricular septum consists of two processes: development of the AV canal occurs via proliferation of the 4 endocardial cushions (superior, inferior, right lateral, and left lateral) and the dextrodorsal conus cushion. As the superior and inferior cushions grow toward each other, the common AV canal becomes two separate and distinct orifices (mitral and tricuspid). The superior and inferior endocardial cushions also extend along the perimeter of the ostium primum, resulting in its closure. Partitioning of the embryonic heart into atrial and ventricular chambers begins at approximately 28 days of gestation. Initially, the interventricular septum forms as a median muscular ridge in the floor of the ventricle near the apex. The early primitive physiologic septal defect that occurs as the septum closes is called the interventricular foramen. Subsequently, the interventricular septum grows and active myoblast proliferation occurs. The free edge of the primitive septum joins with the fused endocardial cushions at approximately 49 days of gestation. The interventricular foramen closes at about 56 days (13).

First trimester screening by nuchal translucency measurements has facilitated early diagnosis of major chromosome abnormality and has also been shown to be a successful means of screening for heart defects in the absence of chromosomal abnormality (13). The poor prognosis of CHD diagnosed antepartum is attributed to the fact that more complex examples are likely to be detected in the fetus. Improvements in screening for fetal heart disease have led to the detection of increasing numbers of cases, including less severe or less complex cases. Our data consisted of six cases in the first trimester, including one case with trisomy 21, diagnosed during screening at 11-14 weeks gestation. Two of the six cases had cystic hygromas, one was born alive with a persistent peri-membranous VSD, aortic regurgitation, and neurologic underdevelopment, and the other case had trisomy 21 and was terminated.

The distribution of the different types of VSDs in our study differs from that of pediatric and prenatal series in the literature. In the pediatric and some prenatal studies, muscular septal defects were more frequent than peri-membranous defects (14-16). In other studies, the incidence of peri-membranous defects was higher than muscular defects (6), which is comparable to our results. Different study populations (prenatal vs. postnatal) and criteria of diagnosis and methods of echocardiography might account for these variations. The detection of muscular defects is facilitated by the pressure gradient existing between the left and right ventricles in the neonate. This determines a high velocity shunt that is easily detected by color Doppler echocardiography. Due to the physiologic patency of the ductus arteriosus and the foramen ovale, this pressure gradient is not present antepartum, rendering the diagnosis of small muscular VSDs very difficult in the fetus. Successful prenatal diagnosis relies primarily on the direct two-dimensional demonstration of the defect, although in some instances flow across small muscular VSDs can be demonstrated by color or pulsed-wave Doppler (6). Our data constituted 69 cases with peri-membranous VSDs and only 18 cases with muscular VSDs, although routine color Doppler use is routine practice in our clinic.

In published reports (17, 18), necropsy studies of live births and stillbirths showed that up to 66% of the cases had more than 1 cardiac anomaly. Our study consisted of 63.3% (n=76) cases with multiple cardiovascular anomalies, which represents a high detection rate of additional cardiac defects.

In the present study, 57 cases (47.5%) with congenital cardiac defects also had extracardiac malformations. The most frequent extracardiac anomalies were found in the central nervous system, musculoskeletal system, gastrointestinal system

and genitourinary system anomalies. Prenatal investigations have shown that heart defects often accompany defects in other organ systems in a wide range of 27%-66% (18-20). These findings point to the need to investigate the heart in cases of extracardiac anomalies and to search for extracardiac anomalies when cardiovascular malformations have been diagnosed. This high proportion of extracardiac anomalies reflects the detailed ultrasonic investigations in fetuses with CHDs, which in many cases led to deliberate termination of pregnancy.

There are different studies showing a wide range of association with chromosomal abnormalities between 5% and 28% (7, 17, 20, 21). The incidence of CHDs and chromosome abnormalities in fetuses is higher than in liveborn infants or stillbirths, as the fetuses often do not survive until birth and are therefore not included in statistical data collected by pediatric cardiologists (21). The frequency of chromosome abnormalities found after the discovery of a CHD varies between 16% (22) and 50% (22). Our data is in agreement with the literature, with an incidence of 18.3% (n=22) of cases associated with cardiac abnormalities. Another interesting point of our study was the relationship between aneuploidy connected to extracardiac and cardiac pathologies. Our results concluded a higher statistical incidence, impact, and relative risk of aneuploidy in the presence of extracardiac abnormalities, then isolated findings of septal pathology or co-existence of other cardiac defects (Table 4).

The present study had some limitations. First, this is a single institute investigation with a low number of pathologies in every subgroup, which causes difficulties in statistical calculation. Second, complete, partial, and intermediate forms of AVSD and inlet, outlet, trabecular, and apical forms of muscular VSD were encountered together. Third, patients requiring surgery were referred to three different cardiac surgery centers in Istanbul. Despite these limitations and the loss of six cases in follow-up, we consider that these data are worth reporting because of the information and differences in prognosis related to AVSDs, and peri-membranous and muscular VSDs. There are many reports in the literature written separately according to AVSD and VSD (peri-membranous and muscular defects together) and related outcomes, but none of them compared these headings together.

The number of cases existing in our series requires to be expanded through larger studies to allow confirmation of the significance of the data from the smaller subclass categories. Despite the small numbers, our study has shown that the risk of aneuploidy is increasing especially in the presence of extracardiac pathologies.

Conflict of interest

None declared

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