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# Prenatal sonographic findings associated with trisomy 13 and 18; report of prenatally diagnosed cases in a single center

## *Trizomi 13 ve 18 ile ilişkili prenatal sonografik bulgular; tek bir merkezde prenatal tanı konmuş olguların sunumu*

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**Abstract**

**Purpose:** In this retrospective study, we aimed to evaluate the prenatal sonographic findings of the fetuses with trisomy 13 and 18.

**Materials and methods:** The sonographic findings of fetuses which were prenatally diagnosed as trisomy 13 and 18 were retrospectively reviewed in two years' period at a single tertiary perinatal center. The most common findings for each aneuploidy were described.

**Results:** Total 13 cases were diagnosed as trisomy 13 or 18 during two years' period of which three cases were trisomy 13 and 10 cases were trisomy 18. Major sonographic abnormality associated with trisomy 13 was holoprosencephaly while cardiac abnormalities were the leading finding for trisomy 18.

**Conclusion:** Trisomy 13 and 18 have major prenatal sonographic findings that may be detected with a targeted sonographic examination. Fetal cardiac and central nervous system abnormalities are the primary major findings associated with trisomy 13 and 18.

**Key words:** Trisomy 18, trisomy 13, prenatal diagnosis.

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**Özet**

**Amaç:** Bu retrospektif çalışmada trizomi 13 ve 18 olan fetüslerin prenatal sonografik bulgularını değerlendirmeyi amaçladık.

**Gereç ve yöntem:** Doğum öncesi 13 ve 18 trizomi tanısı konan fetusların sonografik bulguları, tek bir tersiyer perinatal merkezde iki yıllık dönemde retrospektif olarak incelendi. Her bir anöploidi için en yaygın bulgular tanımlandı.

**Bulgular:** İki yıl boyunca toplam 13 olguya trizomi 13 veya 18 tanısı konuldu, bunlardan üçü trizomi 13 ve 10'u trizomi 18 idi. Trizomi 13 ile ilişkili majör sonografik anormallik holoprosensefali iken kardiyak anormallikler trizomi 18 için önde gelen bulgudur.

**Sonuç:** Trizomi 13 ve 18, sonografik inceleme ile saptanabilecek majör prenatal sonografik bulgulara sahiptir. Fetal kardiyak ve santral sinir sistemi anormallikleri trizomi 13 ve 18 ile ilişkili başlıca bulgulardır.

**Anahtar kelimeler:** Trizomi 18, trizomi 13, prenatal tanı.

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## Introduction

Trisomy 18 also known as Edwards syndrome is a lethal aneuploidy that is caused by the presence of a third copy of all or part of chromosome 18. It is the second most common autosomal trisomy observed in live births (1 in 5500 live births) after trisomy 21 [1]. There is a strong association with advanced maternal age like trisomy 21 due to meiotic nondisjunction. The first description of disorder is made by Edwards et al. [2, 3] in 1960. In utero death of fetuses with trisomy 18 is common due to major fetal systemic abnormalities. Live born babies die in a few days after delivery. Median survival time is <1 month [4]. The presence of major physical abnormalities is almost a rule in trisomy 18 at prenatal sonography. Intrauterine growth retardation (IUGR) combined with polyhydramnios, especially in a fetus with abnormal positioning of hands ("clenched hands"), is strongly suggestive for this disorder [5]. Major structural anomalies associated with trisomy 18 are cardiovascular - central nervous system anomalies, facial, gastrointestinal system and extremity anomalies. Non-structural anomalies include IUGR, increased nuchal translucency, absent-hypoplastic fetal nasal bone, polyhydramnios, single umbilical artery and choroid plexus cysts. Many studies reported at least one abnormal sonographic finding seen in fetuses with trisomy 18 [6].

Patau first described trisomy 13 in 1960 and syndrome is named as Patau syndrome [7]. It is the most common third autosomal trisomy after trisomy 18. Central nervous system anomalies, especially cerebral and facial midline fusion anomalies are remarkable. Polydactyly, single umbilical artery and cardio-renal anomalies are also common. 75% of affected fetuses die in utero due to severe malformations [8]. Since several of these defects can be visualized in the first trimester, detection of trisomy 13 is quite high in the first trimester sonography.

In this article, we reported our experience on prenatal sonographic findings of both chromosomal abnormalities according to the prenatally diagnosed cases in our center.

## Material and methods

This retrospective descriptive study is conducted in Department of Obstetrics and Gynecology, Maternal-Fetal Medicine Unit, Şanlıurfa Education and Research Hospital, Şanlıurfa. Retrospectively collected data was acquired from patients who have undergone to fetal prenatal invasive karyotyping and diagnosed as trisomy 13 or 18, between May 2017 and December 2018. The unit is a busy tertiary center at east of Turkey getting referral patients from the region with approximately 40000-45000 deliveries in a year. Approval and permission for the study about provision of patient data is taken from institutional board. The Medical Ethics Committee of Harran University School of Medicine Ethics Committee approved the trial (Registration number: HRU/20.11.15). The ultrasound device used for the diagnosis and evaluation was a Voluson E8 system (GE Healthcare, Milwaukee, WI). The gestational ages of pregnancies were estimated by either last menstrual period, crown-rump length in first trimester or biparietal diameter with femur length in second trimester. The diagnosis of fetal karyotype was proven by amniocentesis, chordocentesis, or chorion villus biopsy according to the gestational ages at the time of diagnosis. Gestational ages at the diagnosis, method of diagnostic tests, indication for invasive tests and ultrasound findings at the diagnosis were recorded.

Statistical analysis was performed using MedCalc Statistical Software (MedCalc Software, Ostend, Belgium). Statistical analysis was reported descriptively due to small number cases included in the study. Categorical variables were given as median (minimum-maximum).

## Results

After a retrospective analysis of prenatal karyotyping results, 10 cases were identified as trisomy 18 and three cases were identified as trisomy 13 during this 19 months' period. The median maternal age of patients was 33 years (28-46 years). 12 women (92.3%) were multiparous, and 1 (7.8%) was nulliparous. All patients have had been undergone to karyotyping due to fetal abnormal sonographic findings. The diagnosis of abnormal karyotype was not made due to prenatal screening tests in any diagnosed case. Prenatal diagnosis was made by amniocentesis at eight patients, by chordocentesis at three patients and by chorion villus biopsy at two patients. Gestational ages were between 11 and 35 weeks at the diagnosis.

Median gestational age was 15 weeks. Prenatal sonographic findings of trisomy 13 and 18 cases are reported separately in Table 1 and Table 2. Various system anomalies were detected in both trisomy 13 and 18 fetuses. The leading anomalies in the trisomy 13 group were central nervous system anomalies, while that was cardiac anomalies in trisomy 18 group. All patients were offered about termination of pregnancy. Two patients opted to continue the pregnancy and 11 pregnancies were terminated.

**Table 1.** Major sonographic findings of fetuses prenatally diagnosed as trisomy 13

| | Gestational age at diagnosis | Major sonographic findings |
|---|---|---|
| **Case 1** | 11 | Alobar holoprosencephaly |
| **Case 2** | 14 | Alobar holoprosencephaly |
| **Case 3** | 14 | Fetal hydrops, fetal cardiac anomaly |

**Table 2.** Major sonographic findings of fetuses prenatally diagnosed as trisomy 18

| | Gestational age at diagnosis | Major sonographic findings |
|---|---|---|
| **Case 1** | 12 | Fetal hydrops |
| **Case 2** | 12 | Fetal omphalocele |
| **Case 3** | 12 | Increased nuchal translucency |
| **Case 4** | 15 | Fetal omphalocele |
| **Case 5** | 16 | Open spina bifida, Arnold-Chiari type 2 malformation |
| **Case 6** | 19 | Congenital diaphragma hernia, ventricular septal defect, choroid plexus cysts, strawberry shaped head, clenched hand |
| **Case 7** | 19 | Atrioventricular septal defect, clenched hand, club-foot deformity, strawberry shaped head |
| **Case 8** | 22 | Esophageal atresia, truncus arteriosus |
| **Case 9** | 25 | Double-outlet right ventricle, symmetrical intrauterine growth retardation |
| **Case 10** | 35 | Atrioventricular septal defect, symmetrical intrauterine growth retardation |

## Discussion

Trisomy 18 and trisomy 13 are both lethal chromosomal abnormalities result from an extra autosomal chromosome pair. As trisomy 21, there is an association of occurrence with advanced maternal age due to meiotic disjunction [5].

The clinical characteristics of trisomy 18 are first described by Edwards and the disease is named with his name as Edwards syndrome [2]. Multiple organ disorders and malformations are common findings in trisomy 18. Multiple systems are affected and abnormalities at these organ systems make it impossible for newborn to live more than a few days. A major growth retardation starting in early gestation is classic sonographic finding for trisomy 18 [9]. If the organ abnormalities are not detected in first and early second trimester or if the patient did not apply for examination earlier, symmetrical IUGR is a remarkable and prominent finding on sonography. In our study group, diagnosis of fetal trisomy 18 is made at 25 and 35 weeks of pregnancy at two patients due to inadequate prenatal visits. Symmetrical IUGR was the prominent finding at these gestational ages. In addition, cardiac abnormalities were detected in both with a more detailed examination. Although the presence of symmetrical and severe IUGR is significative in the advanced gestational ages, major organ anomalies are the definitive findings in the earlier ages.

Large series of infants with trisomy 18 show that 80%-100% of patients have congenital heart anomalies; ranging from major cardiac

malformations to ventricular and atrial septal defects, patent ductus arteriosus and polyvalvular disease [10-12]. Although in our study, cardiac anomalies were detected only in five of total ten trisomy 18 cases (50%). We think that the reason of this was the too early diagnosis and pregnancy termination of other pregnancies and the difficulty of fetal cardiac examination at first trimester.

The common gastrointestinal defects are common in trisomy 18 and including omphalocele, congenital diaphragmatic hernia (CDH) and esophageal atresia especially with tracheoesophageal fistula. Trisomy 18 is the most common aneuploidy associated with omphalocele [13]. These gastrointestinal anomalies were detected in our cases.

An interesting finding in our study was the association of open spina bifida with trisomy 18. Although the prenatal karyotyping for fetal neural tube defects is controversial, we offer karyotyping to patients with fetal neural tube defects. The interesting one was the neural tube defect was the only sonographic finding at a 16 weeks gestational aged fetus. Stoll et al. [14] reported that aneuploidy rate is 2.5% in 441 neural tube defect cases. Our finding correlates with their results.

Clenched hands, foot deformities and cranial shape abnormalities are common findings in prenatal findings of trisomy 18. These findings should be remarkable at sonographic evaluation. Abnormalities in the extremities and hands were reported in about 95% (36/38) of trisomy 18 fetuses in a study [15]. However, limb abnormalities are being detected in second trimester and this high rate was not present in our study.

Trisomy 13 is rare than trisomy 18 and 21. İntrauterine fetal demise is more than 75% at trisomy 13 fetuses due to severe structural malformations. Since several of these defects can be visualized at 11 to 14 weeks of gestation, first trimester detection of trisomy 13 is high [16]. In our results, all trisomy 13 cases were diagnosed in first trimester due severe major fetal abnormalities.

Craniofacial and cardiac abnormalities are the most common malformations at trisomy 13 fetuses. In addition, the other system malformations can be detected. Because cardiac and cranial abnormalities are severe and can be detected in early gestational ages, the other system anomalies may be detected in second trimester. In our results, three trisomy 13 cases were diagnosed and all were in the first trimester. Holoprosencephaly and cardiac anomalies were the diagnostic findings at sonography. Trisomy 13 accounts for up to 75% of holoprosencephaly cases. Up to 20% of those cases also have triploidy [17].

The major limitation of our study is its retrospective design. In addition, we did not report the findings of aborted fetuses and autopsy results, only prenatal sonographic findings are included. A major strength of this study is that we reported the major sonographic findings that remarked us to make a prenatal invasive test for each gestational age.

In conclusion, trisomy 13 and 18 are severe chromosomal abnormalities that may be suspected with a detailed sonography. Cardiac and cranial malformations are the leading anomalies that are associated with trisomy 13 and 18. If the diagnosis could not be made early in pregnancy, the sonographic abnormalities are more severe and various in the late second trimester.

**Conflict of interest:** No conflict of interest was declared by the authors.

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**Contributions of the authors to the article**

All authors constructed the main idea and hypothesis of the study. EE, ÖÖ, ET and FE. developed the theory and organized the material method section. All authors made the evaluation of the data in the results section. EE wrote the discussion section of the article. All authors reviewed the article, made the necessary corrections and approved. In addition, all authors discussed the entire study and confirmed its final version.