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ORIGINAL ARTICLE

# Retrospective evaluation of amniocentesis results: A tertiary center data

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## ABSTRACT

**Objective:** The aim of this study is to contribute to the literature by retrospectively analyzing the indications, results, culture successes, and pregnancy results of patients who underwent amniocentesis in our clinic between 2021–2022.

**Material and Methods:** Our study includes the results of 132 patients who underwent amniocentesis. Demographic characteristics, weeks of gestation, amniocentesis indications, results, complications, and pregnancy outcomes of the patients were evaluated.

**Results:** In our study, the most common indication for amniocentesis was patients with fetal anomaly detected in ultrasonography (US) with a rate of 38.6% (51/132). The culture success rate was 98.5%. Chromosome anomaly was detected as 18.2% (24/132) in the culture results. Chromosome anomaly was found in 15.7% (8/51) of patients with a fetal anomaly in US. The most common numerical anomalies in culture were Trisomy 21 and Trisomy 18. Among the chromosomal microarray analysis (CMA) results, 4.9% (2/41) were found to be pathogenic and 4.9% (2/41) were classified as variants of uncertain significance (VUS). The pregnancy of 13 patients with chromosomal anomalies was terminated, and three had stillbirths. No maternal or fetal complications related to amniocentesis were observed.

**Conclusion:** Amniocentesis is a reliable and successful prenatal diagnosis test. The results of our study can provide a database for the literature to provide appropriate genetic counseling.

**Keywords:** Amniocentesis, chromosomal abnormality, prenatal diagnosis, ultrasonography.

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## INTRODUCTION

Structural anomalies in the fetus are seen in approximately 3% of live births.[1] Its etiology is based on environmental factors together with genetic factors or the combination of both factors. The risk of chromosomal anomaly and genetic molecular defect increases in fetuses with structural anomalies.[2] It has been determined that fetal chromosomal anomaly is seen at a rate of 2–18% in structurally isolated fetal anomalies and 13–35% in multiple anomalies.[2,3]

Amniocentesis, which is based on the aspiration of amniotic fluid by the transabdominal route, was first performed for the determination of sex cells in the 1950s.[4] Karyotype analysis was started in 1966 by obtaining and culturing the skin and gastrointestinal system cells of the fetus from amniotic fluid.[5]

According to ACOG (American College of Obstetricians and Gynecologists), high risk in first or second-trimester screening tests, abnormality in fetal ultrasonography (US), fetal infections, advanced maternal age, history of habitual abortion, history of a child with a chromosomal abnormality, maternal anxiety, detection of mosaicism in chorionic villus sampling, constitutes some of the indications for amniocentesis.[6]

When amniocentesis is applied in early gestational weeks, the probability of fetal loss is high, and when it is applied after the 20$^{th}$ gestational week, it is usually difficult to reproduce in the amniocyte culture and the result can be obtained in the advancing gestational weeks. It is done between 16-20 weeks of pregnancy.[7]

In this study, our aim is to evaluate the amniocentesis procedures performed between 2021-2022, in our clinic, with indications, desired genetic tests and their results, pregnancy results of patients with chromosomal anomalies and contribute to the literature.

## MATERIAL AND METHODS

In this study, 132 patients who underwent amniocentesis between January 1, 2021, and December 31, 2022, in Van Yüzüncü Yıl University, Department of Perinatology were evaluated. Approval for the study was obtained from the local ethics committee of the Van Yüzüncü Yıl University (Date/number of ethics committee: 14.04.2023/number:2023/04-05). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Demographic characteristics of the patients, indications of amniocentesis, fetal US findings, cytogenetic culture successes, all desired genetic results, and pregnancy outcomes were evaluated retrospectively.

Patients were consulted with the genetics department before the procedure. All patients and their spouses were informed verbally about how amniocentesis was performed before the procedure, its possible complications, and the benefits of the genetic result to be obtained after the procedure. Written informed consent was obtained from the couples who agreed to undergo amniocentesis before starting the procedure. Before the procedure, blood samples were taken from all patients and screened for Hepatitis B, Hepatitis C, and HIV infections. Blood groups were studied from all patients, and 300 mcg Rh IgG was administered intramuscularly to those with Rh incompatibility after the procedure. Prophylactic cefazolin (1 gr) was administered prior to the procedure. Amniocentesis procedures were performed in accordance with the interventional procedures practice guide for prenatal diagnosis published by ISUOG (The International Society of Ultrasound in Obstetrics and Gynecology) in 2016.[8] During the procedure, a convex ultrasound transducer of 2–5 MHz of GE Voluson E6 (General Electric Healthcare, ABD) was used. Ultrasonographic evaluation including placental localization, amniotic fluid amount, and systematic fetal anatomical examination was performed before the procedure. Using a spinal 20 G (BD) needle, the first 2 ml of amniotic fluid was discarded to prevent maternal contamination. Then, a 20 ml amniotic fluid sample was taken with 2 different pistonless injectors and sent to the genetics laboratory. Quantitative fluorescent polymerase chain reaction (QF-PCR) and cytogenetic culture were requested from all patients. Maternal contamination was excluded in all patients by the short tandem repeat sequences (STR) analysis method. During the period when the genetics laboratory was able to work, chromosomal microarray analysis (CMA) and other genetic examinations were performed according to the recommendations of the genetics department. After the procedure, ultrasonographic evaluation was performed for amniotic fluid index, fetal heart rate, and other possible complications.

In the study, for increased nuchal translucency (NT), which is one of our amniocentesis indications, NT measurement according to crown-rump length (CRL) was accepted to be ≥95$^{th}$ percentile.[9]

### Statistical Analysis

While evaluating the findings obtained in the study, SPSS 22 for Windows (Statistical Package for Social Sciences, IBM SPSS Inc.) program was used for statistical analysis. Total count, median, and percentage values are given as descriptive statistics.

## RESULTS

In our study, 132 patients who underwent amniocentesis were found to be a median of 30 years old (range 18–46). The median gestational week at which the procedure was performed was 19+0 (range 15+0-20+6).

The amniotic fluid index was sufficient in 96.2% of the patients on the day of amniocentesis. The placenta was posterior in 51.5% of patients and anterior in 40.9% of patients. An adequate amount of fluid was obtained in 123 (93.2%) patients with a single needle entry and in nine (6.8%) with two needle insertions. Two needle insertions were performed in six patients because they moved during the procedure, causing the angle of the needle to change, and in three patients, the fetal position changed. Ultrasonographic features of the patients and the number of interventions performed on the patients are shown in Table 1.

QF-PCR and chromosome analysis were performed on the samples taken from all patients. During the period when the genetics laboratory was able to work, CMA in 41 patients, molecular deletion duplication analysis for Duchenne Muscular Dystrophy (DMD) in two patients, molecular deletion duplication analysis for Spinal Muscular Atrophy (SMA) in one patient, 22q11.2 deletion analysis by Fluorescent in situ hybridization (FISH) method in four patients, and PTPN11 whole

**Table 1: Ultrasonographic features of the patients and the number of interventions performed on the patients**

| Classification | Number of patient (n) | % |
|---|---|---|
| Pregnancy | | |
| Single | 129 | 97.7 |
| Twin | 3 | 2.3 |
| Amniotic Fluid Index | | |
| Adequate | 127 | 96.2 |
| Polyhydramniosis | 4 | 3.0 |
| Oligohydramnios | 1 | 0.8 |
| Placenta | | |
| Posterior | 68 | 51.5 |
| Anterior | 54 | 40.9 |
| Lateral | 10 | 7.6 |
| Number of puncture | | |
| 1 | 123 | 93.2 |
| 2 | 9 | 6.8 |

**Table 2: Examinations requested from the patients**

| | Number of patient (n) |
|---|---|
| Chromosome analysis | 132 |
| QF-PCR | 132 |
| CMA | 41 |
| 22q11.2 deletion analysis | 4 |
| PTPN11 whole gene analysis | 3 |
| Molecular deletion duplication analysis for DMD | 2 |
| Molecular deletion duplication analysis for SMA | 1 |

CMA: Chromosomal microarray analysis; DMD: Duchenne muscular dystrophy; QF-PCR: Quantitative fluorescent polymerase chain reaction; SMA: Spinal muscular atrophy.

gene analysis for Noonan Syndrome in three patients were studied. The examinations requested from the patients are shown in Table 2.

Fetal structural anomalies were the most common indication for amniocentesis in 51 (38.6%) patients. Eight of them (15.7%) were found to have a chromosomal anomaly. Among the fetal anomalies, 39.2% were central nervous system anomalies, 19.6% were cardiac anomalies, 19.6% were multiple system anomalies, and 11.8% were diaphragmatic hernia anomalies. The second most common indication for amniocentesis was 47 (35.6%) patients with high risk in the combined test, triple screening test, and non-invasive prenatal test (NIPT). A chromosomal anomaly was detected in five (10.6%) of these cases. Increased NT 7.6%, cystic hygroma 5.3%, hydrops fetalis 3.8%, genetic disease in the previous child 3.8%, carrier of genetic disease in the mother 2.3%, multiple soft markers 1.5%, advanced maternal age other amniocentesis indications were 1.5%. The distribution of amniocentesis indications in the patients is shown in Table 3.

**Table 3: Indications of amniocentesis**

| Indication | Number of patient (n) | % |
|---|---|---|
| Fetal structural anomaly | 51 | 38.6 |
| High risk in prenatal triple screening test | 25 | 18.9 |
| High risk in prenatal combined screening test | 20 | 15.2 |
| Increased NT | 10 | 7.6 |
| Cystic hygroma | 7 | 5.3 |
| Hydrops fetalis | 5 | 3.8 |
| Genetic disease in the previous child | 5 | 3.8 |
| Carrier of genetic disease in the mother | 3 | 2.3 |
| Multiple soft markers | 2 | 1.5 |
| Advanced maternal age | 2 | 1.5 |
| High risk in NIPT | 2 | 1.5 |

NIPT: Non-invasive prenatal test; NT: Nuchal translucency.

In QF-PCR, no result could be obtained in one (0.8%) of the patients. Maternal contamination was detected in one (0.8%) patient. Trisomy 21 and 18 were detected most frequently in QF-PCR. The QF-PCR and amniocyte culture results of the patients are shown in Table 4.

Culture results could not be obtained in two (1.5%) patients. The amniocentesis karyotype culture success rate was 98.5%. The rate of chromosomal anomaly in culture results was found to be 18.2% (24/132). Numerical anomalies were detected most frequently with 18 (74.8%) cases among chromosomal anomalies in culture. Trisomy 21 (33.2%) and Trisomy 18 (29.0%) were the most common numerical anomalies. QF-PCR and amniocyte culture results are shown in Table 4, and the distribution of chromosomal abnormalities in culture is shown in Table 5.

Abnormal results were obtained in four (9.8%) of 41 patients for whom CMA was requested. Two (4.9%) of the CMA results were found to be pathogenic and two (4.9%) were in the variant of uncertain significance (VUS) classification.

Hemizygous duplication, which would be compatible with DMD clinic, was found in one of the 10 pregnant women who requested 22q11.2 deletion analysis, PTPN11 whole gene analysis, DMD molecular deletion duplication analysis, and molecular deletion duplication analysis for SMA.

All patients who were found to have chromosomal anomalies as a result of amniocentesis were informed about the prognosis, pregnancy outcomes, and pregnancy termination options. Genetic consultation was requested for all patients. The most common indication for amniocentesis in pregnant women with chromosomal anomalies was anomalies found in the fetus. A total of 13 patients terminated their pregnancies upon their and their husband's request. The pregnancies of three patients with trisomy 21 were terminated

**Table 4: QF-PCR and amniocyte culture results of patients**

| QF-PCR results | n | % | Culture results | n | % |
|---|---|---|---|---|---|
| No aneuploidy | 115 | 87.1 | Normal karyotype | 106 | 80.3 |
| Trisomy 21 | 8 | 6.0 | Numerical anomalies | 18 | 13.7 |
| Trisomy 18 | 7 | 5.3 | Structural anomalies | 4 | 3.0 |
| Maternal contamination | 1 | 0.8 | Structural ve numerical anomalies | 2 | 1.5 |
| No result | 1 | 0.8 | No result | 2 | 1.5 |

QF-PCR: Quantitative fluorescent polymerase chain reaction.

**Table 5: Distribution of chromosomal abnormalities in culture (n=24)**

| Numerical anomalies (74.8%) | | | Structural anomalies (16.8%) | | | Structural ve numerical anomalies (8.4%) | | |
|---|---|---|---|---|---|---|---|---|
| **Results** | **n** | **%** | **Results** | **n** | **%** | **Results** | **n** | **%** |
| Trisomy 21 | 8 | 33.2 | 46....ins(4;2)(q25;p12p2?) | 1 | 4.2 | 47.X*.+mar[2]/46.X*[83] | 1 | 4.2 |
| Trisomy 18 | 7 | 29.0 | 46.X*.der(7)add(7)(q22) | 1 | 4.2 | 47.X*.der(12)i(12)(p10)[79]/46.X*[6] | 1 | 4.2 |
| 45.X[2]/46.X*[77] | 1 | 4.2 | 46.X*.inv(9)(p11q13) | 1 | 4.2 | | | |
| 47.X*.+13[1]/46.X*[134] | 1 | 4.2 | 46.X*.15ps+ | 1 | 4.2 | | | |
| 45.X[1]47.X*.+21[1]/47.X*.+13[1]/46.X*[119] | 1 | 4.2 | | | | | | |

add: Addition; der: Derivative; ins: Insertion; inv: Inversion; mar: Marker chromosome; ps+: Satellite increase in the p arm of the chromosome.

upon their request. Four patients with trisomy 21 gave live birth. A patient who wanted to continue her pregnancy had a stillbirth due to the intrauterine death of the fetus in the third trimester. Pregnancies of five patients with trisomy 18 were terminated upon their request. Two patients with trisomy 18 wanted to continue their pregnancies and had stillbirths due to intrauterine death of the fetuses in the third trimester. Amniocentesis indications and pregnancy results of patients with chromosomal abnormalities as a result of amniocentesis are shown in Table 6.

No maternal and fetal complications related to the amniocentesis procedure were detected.

Of the patients included in our study, 129 (97.7%) were singleton pregnancies and three (2.3%) were dichorionic diamniotic twin pregnancies. Amniocentesis was performed after polyhydramnios, inlet type ventricular septal defect (VSD), and choroid plexus cyst were detected in one baby of one of the twins. Trisomy 18 was detected in the baby with the anomaly. The patient did not accept the selective fetocide procedure. In the follow-up of the patient, the fetus with trisomy 18 was found to be intrauterine exitus at the 28$^{th}$ gestational week. The patient gave birth at term. Amniocentesis was performed because NT increase was detected in one of the fetuses in the other twin pregnancy. Trisomy 21 was detected in the fetus with increased NT. The patient did not accept the selective fetocide procedure. In the follow-up, the patient gave birth at 32 weeks of gestation.

## DISCUSSION

Amniocentesis is usually done for prenatal diagnosis between the 15$^{th}$-20$^{th}$ weeks of pregnancy. It is a more reliable procedure than other diagnostic methods with a 0.1% risk of failed culture and a risk of fetal loss of 0.1%.[8] No fetal or maternal complications were found in our study. Since the complication rate due to amniocentesis is generally low, the evaluation of complications related to amniocentesis in multicenter studies or studies with more participants will enable us to obtain more accurate results.

In our study, the most common indications for amniocentesis were fetal anomalies (38.6%) and high risk in screening tests (35.6%). In a study that included 12,365 patients who underwent amniocentesis, the most common indications for amniocentesis were found to be abnormal screening tests (40.1%), advanced maternal age (34.5%), and anomaly on US (8.1%).[10] In another study evaluating 632 patients who underwent amniocentesis, it was found that abnormal screening tests (72.6%)

**Table 6: Amniocentesis indications and pregnancy outcomes of patients with chromosomal anomaly as a result of amniocentesis**

| Maternal age (year) | Gestational age (week+day) | Indication | Karyotypes | Pregnancy outcome |
|---|---|---|---|---|
| 46 | 15+0 | High risk in NIPT | Trisomy 21 | Termination |
| 43 | 20+0 | High risk in NIPT | Trisomy 21 | Termination |
| 34 | 16+5 (twin pregnancy) | Increased NT in one of the fetuses | One fetus Trisomy 21 + other fetus normal karyotype | Delivery |
| 36 | 16+0 | High risk in prenatal combined screening test | Trisomy 21 | Delivery |
| 34 | 17+0 | High risk in prenatal combined screening test | Trisomy 21 | Delivery |
| 31 | 19+0 | Hypoplastic nasal bone | Trisomy 21 | Termination |
| 22 | 17+1 | Cystic hygroma | Trisomy 21 | Delivery |
| 36 | 17+3 | High risk in prenatal triple screening test | Trisomy 21 | Stillbirth at 36$^{th}$ gestational week |
| 40 | 16+0 | Cystic hygroma | Trisomy 18 | Stillbirth at 34$^{th}$ gestational week |
| 26 | 20+5 | Clubfoot + choroid plexus cyst + polyhydramniosis | Trisomy 18 | Termination |
| 38 | 20+5 (twin pregnancy) | Ventricular septal defect + choroid plexus cyst + polyhydramniosis in one of the fetuses | One fetus Trisomy 18 + other fetus normal karyotype | Anomaly fetus intrauterine ex at 28$^{th}$ gestational week + Other fetus live birth |
| 38 | 20+3 | Hypoplastic nasal bone + clenched hands + polyhydramniosis | Trisomy 18 | Termination |
| 22 | 16+3 | Cystic hygroma | Trisomy 18 | Termination |
| 28 | 20+2 | Ventricular septal defect + choroid plexus cyst + polyhydramniosis + clenched hand + single umbilical artery | Trisomy 18 | Termination |
| 36 | 19+2 | Ventricular septal defect + choroid plexus cyst + polyhydramniosis + clenched hand | Trisomy 18 | Termination |
| 25 | 15+1 | Cystic hygroma + omphalocele | 46....ins(4;2)(q25;p12p2?) + arr[GRCh38] 2p24.2p24.1(18761580-20227386)x1 | Termination |
| 28 | 17+1 | Cystic hygroma + diaphragmatic hernia | 47.X*.der(12)i(12)(p10)[79]/46.X*[6] +arr [GRCh38] 12p13.33p11.1(64.62134.629.700)x4mos | Termination |
| 35 | 17+6 | Paternal DiGeorge Syndrome | arr[GRCh37]22q11.21(18844632_21462353)x1 | Delivery |
| 35 | 18+1 | Dandy-Walker Syndrome | 46.X*.der(7)add(7)(q22) | Termination |
| 24 | 20+5 | High risk in prenatal combined screening test | 45.X[2]/46.X*[77] | Delivery |
| 21 | 20+4 | Open spina bifida | 46.X*.inv(9)(p11q13) | Termination |
| 20 | 16+0 | Maternal DMD carrier | Hemizygous duplication in the DMD gene | Termination |

NIPT: Non-invasive prenatal test; NT: Nuchal translucency; add: Addition; der: Derivative; ins: Insertion; inv: Inversion; DMD: Duchenne muscular dystrophy.

and anomaly detection on US (12.8%) were the most common indications for amniocentesis.[11] In their study, Güven et al.[12] found that the most common indication for amniocentesis was abnormal screening tests, with a rate of 43%. In another study, the most common indication for amniocentesis was found to be abnormal screening tests, with a rate of 29.9%.[13] Fetal structural anomalies were the most common cause of amniocentesis in our study. This may be due to the fact that our center serves as a tertiary center for neighboring provinces and that all anomalies detected in fetuses in these regions were referred to our center.

In our study, the number of pregnant women who underwent NIPT, which has had the highest success among screening tests in recent years, was found to be only two. It was thought that the fact that it was an expensive test in our country and that it was not covered by the social security institution caused it to not be used widely.

In our study, the amniocentesis culture success rate was found to be 98.5%. In their study, Acar et al.,[14] which analyzed 3721 patients, found the culture success rate to be 99.3%, similar to our study. In another study performed by Tao et al.,[15] evaluating 4761 patients, the success rate of culture was found to be 98.3%. Balcı et al.[16] and Gündüz et al.[11] found a culture success rate of 97.9%. The culture success rate in our study is consistent with the literature.

In our study, the rate of chromosomal anomalies was found to be 18.2%, and numerical anomalies were the most common. Acar et al.[14] found the chromosomal anomaly rate to be 3.6%, which is lower than our study. In the same study, similar to our study, it was found that 80.9% of chromosomal anomalies were numerical anomalies and Trisomy 21 was the most common of these. Tao et al.[15] determined the rate of chromosomal anomaly as 2.8% and stated that 89.1% of them were numerical and 10.9% were structural anomalies. Gündüz et al.[11] reported the rate of chromosomal anomaly in their study as 22.4%, similar to our study. In the same study, unlike our study, numerical anomalies were found in 30.2% and structural anomalies in 69%. There are different rates in the studies conducted in the literature. We thought that the indications for performing amniocentesis, the technique of performing amniocentesis, and the rates depending on the laboratory where the material was studied may vary. We thought that the high rate of chromosomal anomaly detected in our study was due to the fact that we are a tertiary center serving a large population and that our most common indication for amniocentesis is fetal anomalies.

There are studies in the literature that found the rate of chromosomal anomaly to be seen in fetuses found to have an anomaly on US between 6.8% and 27.1%.[17,18] The inclusion of soft markers in abnormal US findings in some studies may decrease the rate of detected chromosomal abnormalities. Soft markers were not evaluated as fetal anomalies in our study. We thought that this caused a high rate of chromosomal anomaly in patients who underwent amniocentesis due to fetal anomaly.

Hsiao et al.[19] found chromosomal anomalies in 10.6% of pregnant women and pathological chromosomal anomalies in 2.9% of pregnant women. CMA is especially requested in cases where the fetal anomaly is detected in US. It was thought that the fact that it is an expensive test in our country and that it is not studied in some genetic laboratories caused the test not to be widely used. More studies on CMA will be done as its use becomes more widespread.

The limitation of our study is the lower number of patients compared to some other studies conducted in our country. It was thought that the low number of amniocentesis performed may be due to the region not wanting to have an amniocentesis done due to socio-economic and socio-cultural factors. Obtaining the data from a single center increases confidence in the results and creates the superiority of the study.

## CONCLUSION

In our study, the rate of chromosomal anomaly was found to be 18.2%. Our most common indication for amniocentesis was fetal anomalies detected on US. There were no maternal or fetal complications related to amniocentesis. Amniocentesis is a very reliable and successful prenatal diagnostic test.

### Statement

**Ethics Committee Approval:** The Van Yüzüncü Yıl Clinical Research Ethics Committee granted approval for this study (date: 14.04.2023, number: 2023/04-05).

**Author Contributions:** Concept – HGŞ, MB, KU; Design – HGŞ, EK; Supervision – HGŞ, MB, EK; Resource – MB; Materials – KU; Data Collection and/or Processing – OK, YB; Analysis and/or Interpretation – OK; Literature Search – YB, MB; Writing – MB, KU, YB; Critical Reviews – EK, OK.

**Conflict of Interest:** The authors have no conflict of interest to declare.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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