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Analysis of Amniocentesis Results in a Tertiary Care Center: A Retrospective Cohort Study

Üçüncü Basamak Bir Merkezde Amniyosentez Sonuçlarının Analizi: Retrospektif Bir Kohort Çalışması

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ABSTRACT

Objective: To investigate the results of patients who underwent amniocentesis.

Methods: Information about patients who underwent amniocentesis between May 2021 and May 2022 at the perinatology department of training and research hospital was obtained from the database and evaluated. The demographic characteristics of the patients, indications for amniocentesis, and clinical results of the procedures were also evaluated. Maternal age, gestational age at the time of amniocentesis, amniocentesis indication, and karyotyping results were reviewed and analyzed.

Results: A total of 579 patients were included in the study. The mean ages of the patients and weeks of gestation at the time of the procedure were 32.28 (minimum 17, maximum 50) and 16.32 (minimum 14, maximum 32), respectively. Amniocentesis was most frequently performed in our clinic, with an indication for increased risk according to the dual screening test. Clear chromosome analysis could not be performed using the quantitative fluorescent polymerase chain reaction method in 17 patients, and 38 patients had an abnormal result for long-term cell culture.

Conclusion: Amniocentesis is a frequently used fetal invasive karyotyping procedure. Amniocentesis indications are increasing with the progress of prenatal diagnosis. It is a relatively safe procedure when performed by experienced hands.

Keywords: Amniocentesis, fetal invasive karyotyping, increased risk in screening test, QF-PCR

ÖZ

Amaç: Amniyosentez yapılan hastaların retrospektif olarak değerlendirilmesidir.

Yöntem: Eğitim ve araştırma hastanesiperinatoloji bölümünde, Mayıs 2021 ile Mayıs 2022 tarihleri arasında yapılan amniyosentez vakaları retrospektif olarak değerlendirildi. Hastane veri tabanı incelenerek veriler toplandı. Hastaların demografik özellikleri, amniyosentez endikasyonları, yapılan işlemlerin klinik sonuçları incelendi.

Bulgular: Mayıs 2021 ile Mayıs 2022 tarihleri arasında kliniğimizde toplam 579 hastaya amniyosentez işlemi yapıldı. Hastaların yaşlarının ve işlem anındaki gebelik haftalarının ortalamaları sırasıyla 32,28 (minimum 17, maksimum 50), 16,32 (minimum 14, maksimum 32) olarak saptandı. Amniyosentez işlemi; kliniğimizde en sık ikili tarama testinde risk artışı endikasyonu ile uygulandı. Amniyosentez materyalinden alınan örnekle yapılan kantitatif floresan polimeraz zincir reaksiyonu yöntemiyle yapılan anöploidi taramasında 17 hastanın kromozom analizi net yapılamamıştır. Uzun süreli hücre kültürü sonuçları 38 hastanın anormal olarak tespit edildi.

Sonuç: Amniyosentez sıklıkla uygulanan bir fetal invaziv karyotipleme işlemidir. En sık tarama testlerindeki risk artışı endikasyonları ile yapılır. Tecrübeli eller tarafınca uygulandığında oldukça güvenli bir prosedürdür.

Anahtar Kelimeler: Amniyosentez, fetal invaziv karyotipleme, tarama testinde risk artışı, QF-PCR

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INTRODUCTION

Amniocentesis is used for diagnostic and therapeutic purposes, including chromosomal, biochemical, histopathological, and microbial assessments.[1-3] This process aids families in making informed decisions about continuing the pregnancy, preparing for birth, and understanding the newborn's prognosis while also assisting the physician in diagnosis.[4,5] Counseling should be provided to the family regarding the indications, risks, benefits, and limitations of the procedure.[6]

Although the risks associated with amniocentesis are considered minimal, this procedure is invasive and not entirely free of complications. These complications can include the loss of amniotic fluid during or after the test, fetal injury during the procedure, and pregnancy loss, which is one of the most feared complications. Current studies indicate that the rate of fetal loss related to the procedure is less than 1%.[5,7,8] Recent research shows that the complication rate associated with amniocentesis may depend on factors such as the needle thickness used, whether the puncture is performed transplacentally, the number of punctures, and the experience of the operator. Literature data suggest that at least 30 tests per year are necessary to maintain proficiency and minimize risks associated with practitioner experience.[5,7]

The aim of our study was to examine the indications for amniocentesis, demographic characteristics of patients, and clinical outcomes of amniocentesis in a tertiary hospital.

METHODS

This retrospective cohort study included all patients who underwent amniocentesis at the perinatology clinic of the research hospital between May 2021 and May 2022. Ethical approval was obtained from the Ethics Committee of University Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital Ethics Committee (approval no: 2022/11-24, date: 09.12.2022). Written informed consent was secured from each participant.

Amniocentesis is generally performed in the second trimester. Prior to the procedure, an ultrasound examination is conducted to verify fetal viability, determine gestational age, count the number of fetuses, evaluate placental position, measure amniotic fluid volume, perform fetal anatomical assessment, and identify any uterine cavity abnormalities or fibroids.[9]

The maternal abdomen is disinfected with an antiseptic solution and draped. Due to the possibility of fetal movements altering the locations of amniotic fluid pockets, a larger area of the maternal abdomen is prepped than the designated needle insertion site. A 20-gauge, 9-14 cm long sterile spinal needle is used for the procedure. The ultrasound probe is placed in a sterile cover, with non-sterile gel applied inside and sterile gel on the outside, in contact with the mother's skin. All procedures were conducted by fellows under the supervision of experienced specialists. We use the freehand technique in our clinic, which allows adjustment of the needle entry route. The transducer was held by the fellows while inserting the needle, continuing to visualize the needle tip until an assistant collected the amniotic fluid samples. If the needle tip position is indiscernible on the screen, the needle is not advanced. Using the fellow's wrist, a sudden thrust as the needle passes through the uterine muscle into the amniotic cavity prevents tenting of the membrane.

The extracted amniotic fluid consists of shed fetal cells, transudates, fetal urine, and lung secretions.[7,10-12] As the initial drop of amniotic fluid may contain maternal cells adhering to the needle from the mother's skin, it is discarded to avoid maternal cell contamination in cytogenetic studies. After replacing the syringe, the aspiration of the amniotic fluid was continued. Approximately 20-30 mL of amniotic fluid is aspirated using sterile syringes or vacuum tubes. Several reports have suggested that prolonged contact of the fluid with the syringe stopper can inhibit cell growth in cultures; therefore, we used poisonless syringes to mitigate this risk.

Post-procedure, the fetal heart rate is evaluated and recorded. Patients will be instructed to report any vaginal fluid loss, bleeding, severe uterine cramping lasting for several hours, or fever. There are no restrictions on physical or sexual activity following the procedure. RhD-negative patients who were not alloimmunize will receive Rh(D) immune globulin to prevent RhD sensitization.

Maternal and fetal data were retrieved from the medical records department, including maternal age, indications for amniocentesis, gestational age at the time of amniocentesis, quantitative fluorescent polymerase chain reaction (QF-PCR) results, karyotyping results, and any intra- or postprocedural complications. Data tables were created to calculate mean and median values, including averages for maternal and gestational ages at the time of amniocentesis.

Statistical Analysis

Statistical data were analyzed using the Statistical Package for the Social Sciences software version 26.0. Categorical data were obtained using frequency analysis and are presented as numbers and percentages. Numeric data were obtained by descriptive analysis and presented as means, standard deviations, and minimum-maximum values.

RESULTS

The mean ages of the patients and gestational weeks at the time of the procedure were 32.28 (minimum 17, maximum 50), 16.32 (minimum 14, maximum 32), respectively. Six of the patients who underwent amniocentesis had multiple pregnancies (5 twice, 1 triplet).

Amniocentesis procedure; was performed in our clinic with the most frequent indications of increased risk according to the double screening test in 270 (46.6%) patients, increased risk according to the triple screening test in 59 (10.2%) patients, and maternal anxiety in 37 (6.4%) patients (amniocentesis indications are shown in Table 1). In addition, amniocentesis procedure was performed to affected in previous pregnancy 19 (3.2%) patients, abnormal non-invasive fetal test (NIFT) results in 9 (1.6%) patients, increased risk in quadruple screening test 7 (1.2%) patients, maternal infection in 18 patients (10 toxoplasma, 8 cmv), maternal translocation in 1 patient, carrier of both maternal and paternal muscle disease in 1 patient, and ultrasonographic findings (major fetal anomaly, soft marker) in 158 patients. Details regarding the indications to be affected in previous pregnancy are presented in Table 2.

In the aneuploidy screening performed using the QF-PCR method with the sample taken from the amniocentesis material, a clear chromosome analysis of a total of 20 patients could not be performed; the data are shown in detail in Table 3. The sex chromosomes of 9 patients, the 18th chromosome of 4 patients, the 13th chromosome of 3 patients, and the 21st chromosome of 1 patient could not be made clearly, and contamination was detected in 3 patients.

The final result of 7 cases whose sex chromosome could not be analyzed clearly by QF-PCR was reported as normal karyotype, the definitive karyotype of 1 case was 47 XYY, and the definitive karyotype of 1 case was 47 XXY. In 3 of 4 cases whose chromosome 18 could not be clearly analyzed by QF-PCR, the cytogenetic result was normal karyotype, and Leigh syndrome was detected in 1 case. The final results of 3 cases whose 13th chromosome could not be clearly analyzed by QF-PCR and 1 case whose 21st chromosome could not be clearly analyzed were reported as normal karyotype. The final result of 2 of 3 patients whose QF-PCR result was uncertain due to contamination was a normal karyotype, and the result of 1 patient was 46 der[20]. Long-term cell culture results confirmed trisomy 21 in 11 patients, trisomy 18 in 8 patients, and trisomy 13 in 2 patients. Sex chromosomal anomalies (1 45 X0, 1 47 XXY, 1 47 XYY, 1 47 XXX) were found in 4 patients, structural chromosomal anomaly in 6 patients, and Leigh syndrome in 2 patients.

Table 1. Amniocentesis indications

Indications	Number (n)	Percentage (%)
Increased risk in double-screening	270	46.6
Ultrasonography finding	158	27.28
Increased risk in triple-screening	59	
Maternal anxiety	37	10.2
Affected in previous pregnancy	19	6.4
Abnormal NIFT test result	9	3.2
Increased risk in quad screening	7	1.6
Maternal infection	18	1.2
Maternal translocation	1	3.2
Carrier of both maternal and paternal muscle diseases	1	
Total	579	100

NIFT: Non-invasive fetal test

Table 2. Details regarding the indications to be affected in previous pregnancy

	Number (n)	Percentage (%)
Trisomy 21	6	33
History of trisomy 18	1	5.5
History of trisomy 13	1	5.5
Structural chromosomal anomaly	1	5.5
SMA type 1	3	16.5
Prader-Willi syndrome	1	5.5
Leigh syndrome	2	11
Genetic mutation	2	11
History of triploidy in previous miscarriage	1	5.5
Total	18	100

SMA: Spinal muscular atrophy

The results of 4 patients were unsatisfactory. Mosaicism was detected in 1 patient. The results are presented in Table 4.

No false-positive results were observed for the QF-PCR test. Of the 38 abnormalities detected by cytogenetic analysis, 24 fetuses were diagnosed as chromosomal abnormal (63.15%). A clear analysis of 3 cases with genetic abnormalities could not be performed using QF-PCR test (7.89%). The final result of 7 of 9 cases for which sex chromosome analysis could not be performed by QF-PCR test was normal karyotype and normal sex chromosome, and sex chromosome anomaly (1 patient 47, XXY, 1 patient 47, XXY) was detected in 2 patients. QF-PCR showed 100% specificity for chromosome 21, 18, 13, and X and Y aneuploidies, with 100% positive predictive value and 99.7% negative predictive value. No premature rupture of membranes or vaginal/intrauterine bleeding occurred in the early postoperative period in patients undergoing amniocentesis.

DISCUSSION

Our study identified increased risk in the double screening test as the most common indication for amniocentesis, followed by increased risk in the triple screening test. These findings contrast with those of earlier studies in which advanced maternal age was the predominant indication for the procedure.[13,14] In our study, the second trimester was the most frequent gestational period for amniocentesis, which is consistent with the findings of other studies. The chromosomal anomaly rate in our cohort was 6.5% (38 cases), which is consistent with the rates reported by Ercan et al.[15]

The most prevalent chromosomal abnormality detected was trisomy 21 (Down syndrome), representing 28.94% of cases, followed by trisomy 18 (Edwards syndrome) at 21%, and structural chromosomal abnormalities at 15.78%. Unlike the study by Zhang et al.[16], our study found a higher frequency of structural chromosomal anomalies compared with trisomy 13 (Patau syndrome).

Amniocentesis is an invasive procedure that carries certain risks, such as amniotic fluid leakage, miscarriage, and preterm birth. Procedures performed before 15 weeks are associated with higher rates of fetal loss and complications, including culture failure, and should be delayed if possible.[17] In our study, the mean gestational age during the procedure was 16.32 weeks, and the procedure was performed on three patients after 14 weeks. The cytogenetic results for two of these three patients were unsatisfactory. No cases of premature membrane rupture or vaginal/intrauterine bleeding were observed in the early postoperative period.

Later second-trimester procedures are generally safe, but they may pose challenges if pregnancy termination is planned based on abnormal results. In our study,

Table 3. Quantitative fluorescent polymerase chain reaction; details of cases for which clear chromosomal analysis could not be performed

	Number (n)	Percentage (%)
The sex chromosome cannot be clearly analyzed 18th chromosome could not be analyzed	9 4	45 20
13th chromosome could not be clearly analyzed	3	15
21st chromosome cannot be clearly analyzed	1	5
Contamination	3	15
Total	20	100

Table 4. Patients with abnormal amniocentesis culture results

	Number (n)	Percentage (%)
Trisomy 21	11	28.94
Trisomy 18	8	21
Trisomy 13	2	5
Sex chromosomal anomaly	4	10.52
Structural chromosomal abnormalities	6	15.78
Leigh syndrome Insufficient result	2 4	5.26 10.52
Mosaicism	1	2.63
Total	38	100

amniocentesis was performed in eight patients in the late second trimester. The ethics committee recommended termination for two patients with hydrops fetalis and one patient with multiple anomalies.

Amniocentesis is also used as a therapeutic procedure to reduce amniotic fluid volume in conditions such as symptomatic polyhydramniosis or twin-to-twin transfusion syndrome.[18] In our clinic, amnioreduction was performed in three patients due to polyhydramnios in the last trimester.

The efficacy of prophylactic antibiotics for reducing pregnancy loss associated with amniocentesis has not been comprehensively evaluated. One study involving 33,748 patients randomly assigned to receive azithromycin or no antibiotic treatment before amniocentesis found fewer fetal losses in the prophylaxis group.[19] A single operator conducted all the procedures. During the first 4 weeks post-procedure, the prophylaxis group experienced fewer fetal losses than the control group. Nearly half of the fetal losses (21 out of 43) were associated with preterm prelabor rupture of membranes, which was also less frequent in the prophylaxis group. In our clinic, we administered prophylactic antibiotic therapy to all patients undergoing amniocentesis.

Risk factors for pain during amniocentesis include maternal anxiety, lower uterine needle insertion, history of menstrual cramps, and previous amniocentesis.[20] Local anesthesia is optional and usually unnecessary, as most patients experience no or mild discomfort.[20-23] In our clinic, local anesthesia was not administered to any patients.

The use of simultaneous ultrasound guidance rather than pre-amniocentesis ultrasound evaluation has not been associated with a reduced rate of fetal loss in controlled studies.[3] However, to avoid direct fetal damage and reduce the number of punctures and the possibility of bloody fluid, we perform amniocentesis on all patients with ultrasonographic monitoring, in which the needle is constantly monitored throughout the procedure.

The optimal needle insertion site for amniocentesis should avoid the placenta if possible. Some studies have suggested a higher risk of fetal complications with transplacental amniocentesis, though this has been contested by other studies.[24-35] When a transplacental approach is necessary, there are two options: crossing the placenta or delaying the procedure to allow for a larger intrauterine volume. In our clinic, we preferred the first option of transplacental insertion in 300 out of 579 patients, with no complications observed in either group.

Aneuploidy was detected in five of nine patients who underwent amniocentesis due to abnormal NIFT test results. The amniocentesis QF-PCR and culture results of four patients at high risk of trisomy 21 according to NIFT were consistent with trisomy 21. Four patients with NIFT results indicating a high risk of sex chromosome or structural chromosomal anomalies were found to have normal karyotypes upon amniocentesis. One patient with a high risk of trisomy 13 according to NIFT was confirmed to have trisomy 13 due to a Robertsonian translocation in chromosome 13.

In our study, 536 out of 541 cases diagnosed as having normal karyotype according to long-term cell culture results were confirmed as chromosomal normal by QF-PCR, a rate higher than that reported in the literature.[36] This discrepancy may be due to NIFT not being included in the free national prenatal screening program in our country, leading pregnant women at risk for increased risk for double tests or sonographic markers to seek diagnostic testing.

Study Limitations

Our study has some limitations. It is single-centered and covers the early period in terms of complications.

CONCLUSION

Amniocentesis is a frequently performed fetal invasive karyotyping procedure. It has become increasingly safe with a low rate of pregnancy loss and is considered a reliable and low-risk method for obtaining genetic material. Our results indicate that the procedure is safe and should be offered to all women requesting diagnostic testing, regardless of risk factors or anomalies.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital Ethics Committee (approval no: 2022/11-24, date: 09.12.2022).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: R.T., B.S., S.T.C., C.S., M.Ö., Z.E.Ç., A.G.Ş.Y., A.E., Concept: R.T., Design: R.T., Data Collection or Processing: R.T., B.S., S.T.C., C.S., M.Ö., Z.E.Ç., A.G.Ş.Y., A.E., Analysis or Interpretation: R.T., B.S., Literature Search: R.T., Writing: R.T.

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REFERENCES

1. Piantelli G, Bedocchi L, Cavicchioni O, et al. Amnioreduction for treatment of severe polyhydramnios. Acta Biomed. 2004;75(Suppl 1):56-8.

2. Elliott JP, Urig MA, Clewell WH. Aggressive therapeutic amniocentesis for treatment of twin-twin transfusion syndrome. Obstet Gynecol. 1991;77:537-40.
3. Nizard J. Amniocentesis: technique and education. Curr Opin Obstet Gynecol. 2010;22:152-4.
4. Jummaat F, Ahmad S, Mohamed Ismail NA. 5-Year review on amniocentesis and its maternal fetal complications. Horm Mol Biol Clin Investig. 2019:40.
5. Goto M, Nakamura M, Takita H, Sekizawa A. Study for risks of amniocentesis in anterior placenta compared to placenta of other locations. Taiwan J Obstet Gynecol. 2021;60:690-4.
6. Ramirez-Montiel M, Casillas-Barrera M, Morales-Morales M, et al. Complications associated with amniocentesis in the third trimester of pregnancy. J Clin Gynecol Obstet. 2017;6:34-6.
7. Ghi T, Sotiriadis A, Calda P, et al. ISUOG Practice Guidelines: invasive procedures for prenatal diagnosis. Ultrasound Obstet Gynecol. 2016;48:256-68.
8. Anandakumar C, Wong YC, Annapoorna V, et al. Amniocentesis and its complications. Aust N Z J Obstet Gynaecol. 1992;32:97-9.
9. Ciortea R, Malutan AM, Bucuri CE, et al. Amniocentesis-When It Is Clear That It Is Not Clear. J Clin Med. 2023;12:454.
10. Seeds JW. Diagnostic mid trimester amniocentesis: how safe? Am J Obstet Gynecol. 2004;191:607-15.
11. Porreco RP, Young PE, Resnik R, et al. Reproductive outcome following amniocentesis for genetic indications. Am J Obstet Gynecol. 1982;143:653-60.
12. Wilson RD, Johnson J, Windrim R, et al. The early amniocentesis study: a randomized clinical trial of early amniocentesis and midtrimester amniocentesis. II. Evaluation of procedure details and neonatal congenital anomalies. Fetal Diagn Ther. 1997;12:97-101.
13. Pathompanitrat S, Choochuay P, Wannawat N. Second trimester genetic amniocentesis at secondary center hospital in Southern Thailand. Thai J Obstet Gynecol. 2013;21:134-40.
14. Blackwell SC, Abundis MG, Nehra PC. Five-year experience with midtrimester amniocentesis performed by a single group of obstetricians-gynecologists at a community hospital. Am J Obstet Gynecol. 2002;186:1130-2.
15. Ercan Ö, Köstü B, Arslan G, et al. Does amniocentesis increase the rates of fetal loss and poor pregnancy outcomes? J Clin Anal Med. 2016;7:197-200.
16. Zhang S, Yin M, Xu J, et al. Cytogenetic analysis for fetal chromosomal abnormalities by amniocentesis: review of over 40,000 consecutive cases in a single centre. Reprod Dev Med. 2017;1:84-8.
17. No authors listed. Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. Obstet Gynecol. 2016;127:108-22.
18. Locatelli A, Vergani P, Bellini P, Strobelt N, Arreghini A, Ghidini A. Amnioreduction in emergency cerclage with prolapsed membranes: comparison of two methods for reducing the membranes. Am J Perinatol. 1999;16:73-7.
19. Giorlandino C, Cignini P, Cini M, et al. Antibiotic prophylaxis before second-trimester genetic amniocentesis (APGA): a single-centre open randomised controlled trial. Prenat Diagn. 2009;29:606-12.
20. Harris A, Monga M, Wicklund CA, et al. Clinical correlates of pain with amniocentesis. Am Obstet Gynecol. 2004;191:542-5.
21. Van Schoubroeck D, Verhaeghe J. Does local anesthesia at mid-trimester amniocentesis decrease pain experience? A randomized trial in 220 patients. Ultrasound Obstet Gynecol. 2000;16:536-8.
22. Gordon MC, Ventura-Braswell A, Higby K, Ward JA. Does local anesthesia decrease pain perception in women undergoing amniocentesis? Am J Obstet Gynecol. 2007;196:55.
23. Mujezinovic F, Alfirevic Z. Analgesia for amniocentesis or chorionic villus sampling. Cochrane Database Syst Rev. 2011:CD008580.
24. Tabor A, Philip J, Madsen M, Bang J, Obel EB, Nørgaard-Pedersen B. Randomised controlled trial of genetic amniocentesis in 4606 low-risk women. Lancet. 1986;1:1287-93.
25. Kappel B, Nielsen J, Brogaard Hansen K, Mikkelsen M, Therkelsen AJ. Spontaneous abortion following mid-trimester amniocentesis. Clinical significance of placental perforation and blood-stained amniotic fluid. Br J Obstet Gynaecol. 1987;94:50-4.
26. Bombard AT, Powers JF, Carter S, Schwartz A, Nitowsky HM. Procedure-related fetal losses in transplacental versus nontransplacental genetic amniocentesis. Am J Obstet Gynecol. 1995;172:868-72.
27. Andreasen E, Kristoffersen K. Incidence of spontaneous abortion after amniocentesis: influence of placental localization and past obstetric and gynecologic history. Am J Perinatol. 1989;6:268-73.
28. Reid KP, Gurrin LC, Dickinson JE, Newnham JP, Phillips JM. Pregnancy loss rates following second trimester genetic amniocentesis. Aust N Z J Obstet Gynaecol. 1999;39:281-5.
29. Kalogiannidis I, Prapa S, Dagklis T, et al. Amniocentesis-related adverse outcomes according to placental location and risk factors for fetal loss after midtrimester amniocentesis. Clin Exp Obstet Gynecol. 2011;38:239-42.
30. Crane JP, Kopta MM. Genetic amniocentesis: impact of placental position upon the risk of pregnancy loss. Am J Obstet Gynecol. 1984;150:813-6.
31. Giorlandino C, Mobili L, Bilancioni E, et al. Transplacental amniocentesis: is it really a higher-risk procedure? Prenat Diagn. 1994;14:803-6.
32. Kong CW, Leung TN, Leung TY, et al. Risk factors for procedure-related fetal losses after mid-trimester genetic amniocentesis. Prenat Diagn. 2006;26:925-30.
33. Marthin T, Liedgren S, Hammar M. Transplacental needle passage and other risk-factors associated with second trimester amniocentesis. Acta Obstet Gynecol Scand. 1997;76:728-32.
34. Pitukkijronnakorn S, Promsonthi P, Panburana P, Udomsubpayakul U, Chittacharoen A. Fetal loss associated with second trimester amniocentesis. Arch Gynecol Obstet. 2011;284:793-7.
35. Corrado F, Cannata ML, La Galia T, et al. Pregnancy outcome following mid-trimester amniocentesis. J Obstet Gynaecol. 2012;32:117-9.
36. Cirigliano V, Voglino G, Ordoñez E, et al. Rapid prenatal diagnosis of common chromosome aneuploidies by QF-PCR, results of 9 years of clinical experience. Prenat Diagn. 2009;29:40-9.