Journal of Midwifery & Reproductive Health

JMRH.mums.ac.ir

The Indications of Amniocentesis for the Diagnosis of Aneuploidy among Pregnant Women

Fatemeh Golshahi (PhD)[1], Khosheh Khaleghinezhad (PhD)[2], Behrokh Sahebdel (PhD)[1], Nafiseh Saedi (PhD)[3], Zohreh Salari (MD)[4]*

[1] Assistant Professor, Maternal, Fetal and Neonatal Research Center, Tehran University of Medical Sciences, Yas Hospital, Tehran, Iran
[2] Assistant Professor, Department of Midwifery, Neyshabur Branch, Islamic Azad University, Neyshabur, Iran
[3] Assistant Professor, Department of Obstetrics and Gynecology, Yas Hospital, Tehran University of Medical Sciences, Tehran, Iran
[4] Assistant Professor, Fellowship of Maternal- Fetal Medicine, Department of Medicine, Neyshabur University of Medical Sciences, Neyshabur, Iran

ARTICLE INFO

Article type:
Short Communication

Article History:
Received: 01-Aug-2022
Accepted: 30-Nov-2022

Key words:
Amniocentesis
Aneuploidy
Prenatal Diagnosis

ABSTRACT

Amniocentesis is one of the known and accessible methods for prenatal diagnosis, which is performed for various reasons during pregnancy. The present study was performed to determine the most common reasons for amniocentesis to detect aneuploidy. This retrospective cohort study was performed on the records of 635 pregnant women who underwent amniocentesis guided by high-resolution ultrasound during 2010-2019 at Yas Hospital of Tehran University of Medical Sciences, Tehran, Iran. The study evaluated the indications for amniocentesis in order to investigate the relationship between each of these indications and fetal aneuploidy results. All participants were evaluated for genetic study results. The prevalence of aneuploidy was 8.2% and abnormal screening test was the most common reason for performing amniocentesis (68% of cases). Also, abnormal ultrasound results had the strongest correlation with the possibility of genetic abnormalities in the current pregnancy. Therefore, amniocentesis is highly recommended for women with indications, especially in cases of abnormal ultrasound results.

► *Please cite this paper as*:
Golshahi F, Khaleghinezhad Kh, Sahebdel B, Saedi N, Salari Z. The Indications of Amniocentesis for the Diagnosis of Aneuploidy among Pregnant Women; 2010-2019. Journal of Midwifery and Reproductive Health. 2024; 12(2): 4264-4269. DOI: 10.22038/JMRH.2022.66590.1943

Introduction

Diagnosis of chromosomal abnormalities in the fetus is one of the most important challenges of modern perinatology. Prenatal diagnosis is the best way to avoid the birth of neonates with chromosomal abnormalities (1), and now the capacity to identify them has increased significantly by using molecular methods (2).

Congenital abnormalities and genetic diseases threaten the lives of 3% of neonates (3). Aneuploidy is defined as the presence or absence of one or more chromosomes. Mother's aging increases the risk of fetal aneuploidy. For example, the risk of the birth of a newborn with trisomy 21 (Down syndrome) from 1 in 1,480 at age 20 years increases to 1 in 85 at age 40 years. Although the overall birth rate has decreased in Iran, the age of mothers at the time of first pregnancy has increased. Therefore, all pregnant women should be counseled about aneuploidy screening (4). In study by Bektashian et al. (2016), the risk of aneuploidy was estimated as 6%, the most common form of which was Down syndrome (5).

The major goal of prenatal aneuploidy screening is early detection of high-risk pregnancies with trisomy 21 (Down syndrome), because this syndrome is the most common autosomal trisomy among live births. Since biochemical marker screening for Down syndrome measures the same markers to detect trisomy 18 (Edwards's syndrome, the second most common autosomal trisomy in live births),

* *Corresponding author*; Zohreh Salari, Assistant Professor, Fellowship of Maternal- Fetal Medicine, Department of Medicine, Neyshabur University of Medical Sciences, Neyshabur, Iran. Tel: 00989124768775; Email:drzohrehsslari@yahoo.com

biochemical marker screening tests assess the risk for both chromosomal abnormalities. These screening tests also assess the risk for trisomy 13 (Pateau syndrome) (6).

These screening tests divide mothers into two general groups: low-risk group who do not need another test and high-risk group who are suggested to perform an invasive diagnostic test such as amniocentesis or chorionic villus sampling (7). Although recently non-invasive prenatal DNA test has been limited to trisomy 21, 18, 13 and sex chromosome disorder, but false positive and negative cases cannot be avoided (8). According to the recommendations of the American College of Obstetricians and Gynecologists, women who have a positive screening test should be advised to undergo amniocentesis to determine fetal karyotype. Amniocentesis is one of the well-known and available methods for prenatal diagnosis (3).

The most important reason for performing amniocentesis is to assess the fetal karyotype and chromosomal analysis of amniotic fluid cells. The most important indications of performing amniocentesis for chromosomal and karyotype evaluation are: (1) maternal high age during pregnancy (≥35 years), (2) history of chromosomal abnormalities in previous pregnancies, (3) abnormal screening result in the first or second trimester of pregnancy (4) positive family history of chromosomal or genetic disorder, (5) parents' carriers of one of the chromosomal abnormalities (6) Abnormal findings in ultrasound anomaly scan (9-10). Other indications include evaluating fetus for infection, hemolytic anemia, hemoglobinopathy, and neural tube defects. Assessment of fetal lung maturity, which was a common indication for amniocentesis, is now rarely performed (10).

In a study in China, Zhang and colleagues (2017) examined fetal chromosomal abnormalities through amniocentesis. Abnormal result of maternal serum screening was the most common indication for amniocentesis (43.67%), abnormal ultrasound findings and maternal request were in the next ranks. Abnormal karyotype was detected in 3.36% of cases, 63% of which were associated with number disorders and 37% were associated with chromosomal structural disorders. The highest rate of chromosomal disorders was detected in couples who one of them had a chromosomal disorder (55.6%) (11). The most common complications of amniocentesis include premature rupture of membranes, direct and indirect fetal injuries, infection, abortion and amnionitis, uterine contractions and temporary spotting. Also, the risk of spontaneous pregnancy loss following amniocentesis is estimated as 0.06 to 1% (12). Since amniocentesis is still considered a new method in Iran, so this study was performed to examine the indications of amniocentesis in the diagnosis of aneuploidy.

Materials and Methods

This retrospective cohort study was conducted on the records of 635 pregnant mothers who underwent amniocentesis in Yas Hospital of Tehran University of Medical Sciences during 2010-2019. The reason for choosing this time period was the availability of hospital records. These patients with various indications, including abnormal screening results in the first or second stage screening test, history of a child with aneuploidy or genetic problems, structural abnormalities in ultrasound, or at the request of mother were consulted at the prenatal clinic and were candidates for amniocentesis. Therefore, about 7200 records were examined and the cases with incomplete data were excluded from the study, and finally 635 cases were included.

All patients were visited under the supervision of one of the three faculty members who were fellowships in perinatology. The possible complications were explained to pregnant women candidates for amniocentesis and a consent form was obtained. Then amniocentesis was performed using a 20 gauge spinal needle under high resolution ultrasound guidance (ACUSON Sequoia 512™, Siemens Healthcare GmbH and USA). All participants were evaluated for genetic disorders by chromosomal culture. Then the results of amniocentesis were examined and demographic information, indications of amniocentesis and their relationship with genetic results were evaluated. Data were analyzed by SPSS (version 22). The results were presented using descriptive and inferential statistics. In the

Results

A total of 635 pregnant women underwent amniocentesis, the mean age of these women was 33.4 ± 5.7 years, and the mean gestational age at the time of amniocentesis was 17.3 ± 1.5 weeks (Table 1).

Table 1. Demographic characteristics of mothers undergoing amniocentesis

Variable	Rate
Mean maternal age (yrs)	33.4 ± 5.7
Average gestational age at the time of amniocentesis (weeks)	17.3 ± 1.5
Spontaneous pregnancy rate	530 Cases (83.5%)
The rate of use of assisted reproductive methods (ART)	21 Cases (3.3%)
Pregnancy rate using medication	84 Cases (13.2%)
Mean BMI of mothers (Kg/m2)	26.8 ± 4.2
Parity (pregnancy)	2.2 ± 1.3
A history of at least one miscarriage	59 Cases (9.3%)
History of fetal anomaly or aneuploidy in previous pregnancy	52 Cases (8.2%)

Table 2. The most common indication for performing amniocentesis

The indications of amniocentesis	P	The number of cases of genetic abnormalities in each group	The proportion of people with genetic abnormalities in each group
Abnormal screening results	432 (68%)	33	7.64
Mother's request	76 (12%)	7	9.21
Abnormal ultrasound results	75 (11.8%)	8	10.67
*History of a genetic problems in parents or other child	52 (8.2%)	4	7.69

* Genetic defects in parents are very diverse, which is mentioned under the general title of history of any abnormal genetic results in parents

Table 3. The proportions equality test for the different indications of amniocentesis

The indications of amniocentesis	Abnormal screening results		Mother's request		Abnormal ultrasound results		History of a genetic problems in parents or other child	
Abnormal screening results	95%CI	–	95%CI	0.208-0.374	95%CI	0.004-0.227	95%CI	-0.207-0.392
	p-value	–	**p-value**	0.000	**p-value**	0.042	**p-value**	0.000
Mother's request	95%CI	0.208-0.374	95%CI	–	95%CI	-0.052-0.298	95%CI	-0.097-0.115
	p-value	0.000	**p-value**	–	**p-value**	0.005	**p-value**	0.866
Abnormal ultrasound results	95%CI	0.004-0.227	95%CI	-0.052-0.298	95%CI	–	95%CI	-0.054-0.313
	p-value	0.042	**p-value**	0.005	**p-value**	–	**p-value**	0.005
History of a genetic problems in parents or other child	95%CI	-0.207-0.392	95%CI	-0.097-0.115	95%CI	-0.054-0.313	95%CI	–
	p-value	0.000	**p-value**	0.866	**p-value**	0.005	**p-value**	–

In the investigation of the chromosomal cultures, 52 of these women (8.2%) had a QF-PCR test disorder (Quantitative Fluorescence Polymerase

Chain Reaction), which was also confirmed in the chromosomal culture. Abnormal screening results were the most common indication for amniocentesis (68.4%), and mother's request and abnormal ultrasound findings were in the next rank (Table 2).

Examining the different indications for amniocentesis showed the highest rate of diagnosis of chromosomal disorders following abnormal ultrasound results (Table 3).

Discussion

The findings of this study showed that abnormal screening test was the most common reason for performing amniocentesis and abnormal ultrasound results had the strongest correlation with the possibility of genetic abnormalities in the current pregnancy. Therefore, performing amniocentesis to reduce congenital defects in prenatal diagnosis is considered an important and logical approach.

However, little is known about the personal and family risks of screening, it is normal to be worry about the adverse psychological effects including fear of detecting an infected fetus and the complications of diagnostic and therapeutic interventions, especially the loss of a normal fetus. Most parents are anxious about the results of screening test, even the screening results are normal pregnancy outcome (13). Women may also be concerned about false negative results; on the other hand, there is a possibility that the screening will not detect an affected fetus (14).

Krapp et al. (2017) in a study titled "Indications for Fetal Invasive Procedures at the End of an Era" showed that only 8% of amniocentesis samples were associated with an abnormal karyotype (15). This rate in the study of Hassanzadeh et al. (2013) was 11 out of 121 samples (9.1%) with aneuploidy (3). This rate was 8.2% in the present study, which was similar to other studies. In the present study, the most common reason for performing amniocentesis was abnormal screening test results, which was consistent with the results of Zhang et al.'s (2017) study (11). In the study of Ali Akbari and Tooba (2019), titled "Analyzing indications of amniocentesis and positive predictive value (PPV) of cytogenetic findings of chromosomal abnormalities" which was performed on 715 cases, the most common reason for performing amniocentesis was a positive result in the screening of mother's serum (9). While Daum et al. (2019) in a study entitled "Role of late amniocentesis in the era of modern genomic technologies" showed that the most common indication for performing late amniocentesis (24 to 38 weeks) was abnormal ultrasound findings (67% of cases) (16), which corresponded to the third priority in our study with a slight difference compared to the second rank, and the reason for this difference seems to be the different time of the amniocentesis in these studies.

In the present study, abnormal ultrasound result was the strongest factor associated with abnormal amniocentesis results, while in the study of Zhang et al. (2017), titled "Cytogenetic analysis of fetal chromosomal abnormalities by amniocentesis", the strongest predictor was genetic abnormalities in one of the parents (55.6%) (17) Which is due to the difference of the population in two studies.

Maternal age alone is a poor standard for prenatal aneuploidy screening and should not be the basis to recommend invasive test when there is noninvasive prenatal screening for aneuploidy (6). For this reason, the mother's age alone was not used as a basis for performing the procedure in this study, but if the mother requested and amniocentesis was performed after adequate counseling and informing the person and the total data didn't support its positive relationship with abnormal amniocentesis results. On the other hand, invasive prenatal diagnosis for cytogenetic analysis should not be done without screening of multiple markers, except for women who are at higher risk of fetal aneuploidy due to ultrasound findings (6), and the results of this study also showed a strong relationship between the abnormal ultrasound findings and genetic disorders followed by amniocentesis.

The limitations of the present study included incomplete data in the files, especially the files before 2015, the different people performing the amniocentesis, and no knowledge of the results of some amniocentesis due to the transfer of the

patient to other centers and cities. One of the strengths of this study was the large sample size and a large time period in a referral center. It is suggested that another study be designed by determining the types of genetic abnormalities and following the results of births with a comprehensive information system.

Conclusion

Abnormal screening results were the most common indication for performing amniocentesis, mother's request and abnormal ultrasound results were in the next rank. The detection rate of abnormal karyotype was 8.2%. The highest rate of diagnosis of chromosomal disorders was obtained after abnormal ultrasound results. The results of fetal amniocentesis in the current study indicates the importance of genetic screening tests in pregnant women, therefore performing amniocentesis is strongly recommended for women with indications, especially in cases of abnormal ultrasound results.

Acknowledgements

This article was extracted from the thesis of Maternal and Fetal Medicine fellowship with code 1400-430-2-52603 and under ethics code IR.TUMS.MEDICINE.REC.1400.831, which has been approved by the Vice President for Research and Ethics Committee of Tehran University of Medical Sciences. Finally, the authors express their gratitude to all those who helped us in conducting this study.

Conflicts of interest

Author declared no conflicts of interest.

References

1. Naghizadeh S, Azari S, FathNeghad Kazemi A, Ebrahimpour Mirza Rezaie M, SH. A. Assessing and comparing result of amniocentesis and tripl marker tests to detection of aneuplodies. E Journal of Urmia Nursing and Midwifery Faculty. 2015; 13(7): 596-604.
2. Wojcik M, Reimers R, Poorvu T, Agrawal P. Genetic diagnosis in the fetus. Journal Perinatol. 2020; 40(7): 997-1006.
3. Hasanzadeh R, Naghizadeh S, Azari S, M. EMR. Diagnosis of Aneuploidies by amniocentesis in high risk cases of first trimester screening test. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2014; 17(119): 18-26.
4. LeFevre N, Sundermeyer R. Fetal Aneuploidy: Screening and Diagnostic Testing. American Family Physician. 2020; 101(8): 481-488.
5. Baktashian M, Sedghi M, Salehi M, Mirlohi F, Zarean E, Baghersad A, et al. Study of prenatal screening tests in pregnant women and comparison with fetal karyotype results. The Iranian Journal of Obstetrics, Gynecology and Infertility. 2018; 20(11): 22-28.
6. Chitayat D, Langlois S, Wilson R. Prenatal screening for fetal aneuploidy in singleton pregnancies. Journal of Obstetrics and Gynaecology Canada. 2011; 33(7): 736-750.
7. Cunningha F, Leveno K, Bloom S, Dashe J, Hoffman B, Casey B, et al. Williams Obstetrics. 25rd Ed. New York: McGraw-Hill; 2018.
8. Snyder MW, Simmons LE, Kitzman JO, Coe BP, Henson JM, Daza RM, et al. Copynumber variation and false positive prenatal aneuploidy screening. The New England Journal of Medicine. 2015; 372(17): 1639-1645.
9. Ali Akbari N, Tooba K. Analyzing indications of amniocentesis and positive predictive value (PPV) of cytogenetic findings of chromosomal abnormalities. Revista Latinoamericana de Hipertensión. 2019; 14(3): 313-319.
10. Ghidini A. Diagnostic amniocentesis: Uptodate; 2021 [Available from: https://www.uptodate.com/contents/diagnostic-amniocentesis.
11. Zhang S, Yin M, Xu JZ, Lei CX, Wu JP, Sun XX, et al. Cytogenetic analysis for fetal chromosomal abnormalities by amniocentesis :Review of over 40,000 consecutive cases in a single center. Reproductive and Developmental Medicine. 2017; 1(2): 84-88.
12. Tara F, Moeindarbari S, Bakhtiari M. Investigating the Complications of Transplacental Needle Passage in Amniocentesis. Journal of Mazandaran University of Medical Sciences. 2019; 29(17): 24-30.
13. Lou S, Mikkelsen L, Hvidman L, Petersen O, Nielsen C. Does screening for Down's syndrome cause anxiety in pregnant women? A systematic review. Acta Obstetricia et Gyn
14. Kupp ecologica Scandinavica. 2015; 94(1): 15-27. ermann M, Pena S, Bishop J,

15. Nakagawa S, Gregorich S, Sit A, et al. Effect of enhanced information, values clarification, and removal of financial barriers on use of prenatal genetic testing: a randomized clinical trial. Journal of the American Medical. 2014; 312(12): 1210-1217.
16. Krapp M, Thomsen Y, Ludwig A, Enzensberger Ch, Ph .K. Indications for Fetal Invasive Procedures at the End of an Era. Ultraschall in der Medizin / European Journal of Ultrasound. 2017; 38(1): 78-82.
17. Daum H, Ben David A, Nadjari M, Zenvirt S, Helman S, Yanai N, et al. Role of late amniocentesis in the era of modern genomic technologies. Ultrasound in obstetrics & Gynecology. 2019; 53(5): 676-685.
18. Zhang S, Yin M, Xu JZ, Lei CX, Wu JP, Sun XX, et al. Cytogenetic analysis for fetal chromosomal abnormalities by amniocentesis: Review of over 40,000 consecutive cases in a single center. Reproductive and Developmental Medicine. 2017; 1: 84-88.