Amniocentesis Following Positive First Trimester Combined Screening: A Comparative Study

Fakhrolmolouk Yassaee[1], Reza Shekarriz-Foumani[2], Shima Sadeghi[3]

[1] *Department of Obstetrics and Gynecology, Genomic Research Center, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[2] *Department of Community Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[3] *Department of Electrical, Biomedical and Mechatronics Engineering, Qazvin Branch, Islamic Azad University, Qazvin, Iran*

Received: 22 Feb. 2019; Accepted: 7 Jun. 2019

Abstract- The birth of a neonate with chromosomal abnormalities, e.g. Down syndrome has very serious problems for family, society, and for the neonate itself, and therefore prenatal evaluation is imperative in determining the fate of the fetus. This research aimed to assess the association and accuracy of amniocentesis with first-trimester combined screening. In this study, specimens from 1066 cases were analyzed for free Beta human chorionic gonadotropin, pregnancy-associated plasma protein A, along with nuchal translucency and nasal bone ultrasonography from October 2013 till November 2014. Upon observing positive screening, mothers underwent amniocentesis. Finally the amniocentesis results were compared with that of first-trimester screening. Our results determined a direct relation between the high age of the mother and gravidity with *P* of 0.001 and 0.020 with positive first-trimester screening. Our study attained a 92% accuracy rate of amniocentesis due to one case of mosaicism of trisomy 21, that was not diagnosed, because it was not requested by physician. Only 12 (17.1%) cases out of 70 (mothers with positive first-trimester screening) showed positive amniocentesis, which had a significant relationship with chromosomal abnormality. First trimester combined screening has very high accuracy (94.6%) in prediction of genetic abnormalities. The probability of positive first-trimester screening is directly influenced by number of factors, including the mother age and gravidity. Amniocentesis is necessary for all of mothers with positive first-trimester screening and will almost always detect chromosomal abnormalities.

Acta Med Iran 2019;57(6):359-362.

Keywords: Pregnancy first trimester; Amniocentesis; Prenatal diagnosis

Introduction

Nowadays, increasing age of marriage and pregnancy, health conditions such as hypertension, diabetes, obesity, exposure to teratogenic factors such as alcohol and viral infections cause high-risk pregnancy and increase the chance of having a child with chromosomal anomalies. Women performing difficult jobs or completing university tasks often get married too late. The increase in marriage age poses a risk for chromosomal defects. For all pregnancies, the baseline risk of some type of birth defect is 3-4%. Therefore prenatal diagnosis of fetal aneuploidy is very important. Ultrasonography is for diagnosis of fetal structural abnormalities, but for diagnosis of chromosomal anomalies adding biochemistry to nuchal translucency greatly improved detection rate and decreased false-positive rates for patients requesting early screening (1). The benefits of first-trimester screening over second-trimester screening include reduced anxiety for patients due to early availability of results, as well as the provision of diagnostic tests for those at increased risk. In case of patients with confirmed abnormal karyotype, first-trimester abortion is safer (2,3). Due to high cost of raising disabled children and the socio-economic burden of rare diseases it is mandatory to prevent the delivery of such babies. First-trimester screening not only identifies pregnancies at risk of fetal aneuploidy but also provides insight into other adverse pregnancy outcomes such as fetal death, cardiac defects, and fetal infections (4). In this

Corresponding Author: F. Yassaee
Department of Obstetrics and Gynecology, Genomic Research Center, Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel: +98 912 1262358, Fax: +98 21 22433581, E-mail address: Dr.fyassaee1956@gmail.com

study, we compared the outcome of first-trimester screening with the results of amniocentesis in Iranian pregnant women.

Materials and Methods

This study was a retrospective cohort study of all patients seen for first-trimester screening from October 2013 through November 2014. All patients requesting first-trimester screening were offered combined screening with nuchal translucency and biochemistry (PAPP-A and free Beta HCG) between 11w, 2d-13w, 6d of gestation (using cut off value of 1/250). Biochemical testing for PAPP-A and free Beta HCG was available through reference laboratory. They were also scheduled for an NT ultrasonography by a certified sonographer on day of collecting the blood sample. Nuchal translucency measurements were obtained in the standard fashion as described in the Fetal Medicine Foundation protocol. Results of that ultrasound (nuchal translucency and crown-rump length) were then combined with biochemical results. Combined results were provided to the patients. Limitations and options for further screening or for diagnostic testing were again reviewed. In patients who screened positive, amniocentesis was offered. Categorical outcomes were examined with the Chi-square test. Statistical significance was determined by a $P<0.05$.

This study was approved by the Shahid Beheshti University of Medical Sciences Committee. Cut off for a positive screen was 1:250.

Results

During study period 1066 women were seen for first-trimester screening. The mean age of women was 27.18±5.4 years. The mean age in women with positive screening was 30.59±4.7, and the mean age in women with negative screening was 26.56±4.2 years. According to T-test examination the difference was significant (P=0.001). Of 1066 women, 555(52.1%) women were gravida 1 from which 32(5.8%) were positive. The gravida 2 women were 351(32.9%), of which 17(4.8%) women were positive, and 334(95.2%) were negative. The numbers of gravida 3 women were 129(12.1%), of which 15(11.6%) were positive, and 114(84.4%) were negative. The gravida 4 women were 25(2.3%), and 5 women were gravida 5(0.5%). Pearson *Chi*-Square examination showed significant P 0.02 between gravidity and positive screen test. Of 1066 women, 495(46.4%) women had normal BMI and 470(44.1%) were overweight, and 101(9.5%) were obese. The number of women with normal BMI who had positive screen tests were 38(7.7%), and 457(92.3%) women had negative screen tests. The number of overweight women with positive screen tests were 25(5.3%) who had positive screen, and 445(94.7%) women had negative screen tests. Pearson *Chi*-Square test showed no significant relation between BMI and positive screen (P=0.332). Of 1066 women requesting first-trimester screening, 70(6.6%) women had positive screen tests and were referred for amniocentesis. According to the results of amniocentesis, 12(17.1%) women revealed abnormal karyotype, of which 10(83.3%) with Down syndrome, 1(8.35%) with trisomy 13 and 1(8.35%) with trisomy 18. The false-positive result for first-trimester screening was 5.4%, and its accuracy was 94.6%. All 12 women with abnormal karyotype in amniocentesis gave birth to infants with chromosomal abnormalities. Hence indicating a statistically significant association between result of amniocentesis and delivery of fetus with chromosomal abnormalities (P<0.001). Only one neonate delivered with abnormal chromosome and normal karyotype in amniocentesis. Thus, the sensitivity of amniocentesis was 92%. This case was mosaicism of trisomy 21, and because of no request for doing that, the neonate was delivered with this syndrome.

Discussion

This study showed that first trimester combined screening is an effective screening test for prediction of chromosomal abnormalities such as Down syndrome and is corresponded with studies conducted in other countries (1,9-19). Amniocentesis could diagnose abnormal karyotypes and prevent delivery of babies with abnormal chromosomes. Our investigations detected chromosomal aberrations in 17.1% of which 83.3% were Down syndrome thereby opposing an earlier study from Taiwan by Chih-Ping Chen *et al.*, stating that chromosomal aberrations were detected in only 2.53% of which 30.28% were down syndrome, consequently underestimating the significant impact of amniocentesis in the detection of down syndrome (7). Our study is in agreement with other studies emphasizing the critical role of first-trimester screening in detection of down syndrome and the declination of invasive procedures (1-4). Following a positive screening test, a diagnostic procedure to confirm the result is strongly recommended, (5). Another study by Seyyed Kavoosi E *et al*., in 2015 revealed that the detection rate for DS in three groups was as follow: 87.5% for FTS (25783 women), 80.9% for STS (91345 women), and 94.7% for combined tests (8042 women) (14), however

we detected DS cases with 94.6% sensitivity in first trimester. Nicolaides in 2004 tabulated that nuchal translucency, PAPP-A, and HCG detected 87% of trisomy fetuses in which the false positive rate was set at 5% (1), that is also comparable with our study with detection rate of 94.6% and false-positive rate of 5.4% . A study from India in 2016 showed the sensitivity of the prenatal screening using the combination of maternal age, and fetal nuchal translucency for fetal trisomy 21 was 75% and for all fetal aneuploidy was 80% (8), but in our study the sensitivity of the first trimester screening was 94.6% for prediction of the fetal aneuploidy. Another study by Rydberg and colleagues showed that abnormal fetal anomaly was diagnosed by second-trimester sonography (6). The high detection rates in our study may be due to chemical tests (PAPP-A, free Beta HCG) that were involved in addition to maternal age and fetal nuchal translucency.

The current study confirms that the first trimester combined screening with the use of maternal age, nuchal translucency, and the biochemical markers drastically reduce the number of women who may need CVS or amniocentesis for prenatal diagnosis. The most important point is that for all specimens the physician must request the karyotype and mosaicism of trisomy 21.

Table 1. The relation between demographic data and first trimester combined screening

Characteristics	Total (n=1066)	screen negative (n=996)	Screen positive (n=70)	*P**
Age	27.18±4.54	26.56±4.2	30.59±4.70	0.001
Gravid				0.02
	555 (52.1)	523 (94.2)	32 (5.8)	
	351 (32.9)	334 (95.2)	17 (4.8)	
	129 (12.2)	114 (84.4)	15 (11.6)	
	25 (3.2)	21 (84)	4 (16)	
	5 (0.5)	4 (80)	1 (20)	
Previous abortion	173 (16.2)	195 (91.1)	14 (8.1)	0.376
BMI				0.332
Normal	495 (46.4)	457 (92.3)	38 (7.7)	
Overweight	470 (44.1)	445 (94.7)	25 (5.3)	
Obese	101 (9.5)	92 (91)	9 (9)	
Parity				0.077
	630 (59.1)	594 (94.3)	36 (5.7)	
	365 (34.2)	342 (93.7)	23 (6.3)	
	61 (5.7)	53 (86.9)	8 (13.1)	
	9 (0.8)	8 (88)	1 (12)	
	1 (0.1)	1 (100)	0 (0)	

BMI: Body mass index
**P* less than 0.05 were considered as statistically significant

Table 2. The relation between demographic data and amniocentesis

	Positive amniocentesis (n=12)	Negative amniocentesis (n=58)	*P**
Age	30.08±4.4	30.69±4.8	0.692
BMI	24.7±3.8	24.9±3.9	0.873
Gravid			0.096
	5 (15.6)	28 (84.4)	
	6 (35.3)	11 (64.7)	
	1 (6.7)	14 (93.3)	
Parity			0.449
	5 (13.9)	31 (86.1)	
	6 (26.1)	17 (73.9)	
	1 (12.5)	7 (87.5)	

BMI: Body mass index
* *P* less than 0.05 were considered as statistically significant

References

1. Wu N, Platt LD, Greene N, Currier RJ. Practitioner–Specific Medians for Nuchal Translucency to Improve First-Trimester Screening Performance. Obstet Gynecol 2012;119:785-94.

2. Baer R, Flessel M, Jelliffe-Pawlowski L, Goldman S, Hudgins L, Hull A, et al. 216: Detection of chromosome abnormalities by sequential screening with first and second trimester serum and nuchal translucency. Am J Obstet Gynecol 2015;212:121-2.
3. ER P, NA IJR. Results of routine first trimester screening tests and following invasive procedures during pregnancy. Perinat J 2015;23:50-5.
4. Fang YMV, Benn P, Campbell W, Bolnick J, Prabulos AM, Egan JF. Down syndrome screening in the United States in 2001 and 2007: a survey of maternal-fetal medicine specialists. Am J Obstet Gynecol 2009;201:1-5
5. Zelig CM, Knutzen DM, Ennen CS, Dolinsky BM, Napolitano PG. Chorionic Villus Sampling, Early Amniocentesis, and Termination of Pregnancy Without Diagnostic Testing: Comparison of Fetal Risk Following Positive Non-invasive Prenatal Testing. J Obstet Gynaecol Can 2016;38:441-5.
6. Rydberg C, Tunón K. Detection of fetal abnormalities by second-trimester ultrasound screening in a non-selected population. Acta Obstet Gynecol Scand 2017;96:176-82.
7. Lan R-Y, Chou C-T, Wang P-H, Chen R-C, Hsiao C-H. Trisomy 21 screening based on first and second trimester in a Taiwanese population. Taiwan J Obstet Gynecol 2018;57:551-4.
8. Chaudhury K, Mukherjee K. Sensitivity and specificity of a prenatal screening method using the combination of maternal age and fetal nuchal translucency thickness for fetal aneuploidy: a clinical study in eastern India. Int J Reprod Contracept Obstet Gynecol 2016;5:148-53.
9. Liu Y, Ye X, Zhang N, Zhang B, Guo C, Huang W, et al. Diagnostic value of ultrasonographic combining biochemical markers for Down syndrome screening in first trimester: a meta-analysis. Prenat Diagn 2015;35:879-87.
10. Sequeira S, Uppal S. Prenatal screening for fetal aneuploidies during the first and second trimester of pregnancy. Hamdan Med J 2013;212:1-12.
11. Rose NC, Lagrave D, Hafen B, Jackson M. The impact of utilization of early aneuploidy screening on amniocenteses available for training in obstetrics and fetal medicine. Prenat Diagn 2013;33:242-4.
12. Singh N. Screening for Fetal Aneuploidy. Screening in Obstetrics & Gynecology: Management of Abnormalit. 1th ed. New Delhi, India: Jaypee Brothers,2015.
13. Spencer K. Screening for Down syndrome. Scand J Clin Lab Invest 2014;74:41-7.
14. Seyyed Kavoosi E, Younessi S, Farhud DD. Screening of Fetal Chromosome Aneuploidies in the First and Second Trimester of 125,170 Iranian Pregnant Women. Iran J Public Health 2015;44:791-6.
15. Shajpal A, Siddiqui F. Screening for Down syndrome. Obstet Gynecol Reprod Med. 2017;27:333-7.
16. Chitayat D, Langlois S, Wilson RD, Audibert F, Blight C, Brock J-A, et al. Prenatal screening for fetal aneuploidy in singleton pregnancies. J Obstet Gynaecol Can 2011;33:736-50.
17. Tørring N, Petersen OB, Uldbjerg N. Ten years of experience with first-trimester screening for fetal aneuploidy employing biochemistry from gestational weeks 6+ 0 to 13+ 6. Fetal Diagn Ther 2015;37:51-7.
18. Nicolaides KH. Screening for fetal aneuploidies at 11 to 13 weeks. Prenat Diagn 2011;31:7-15.
19. Källén B. Genetic and Non-genetic Factors in the Origin of Congenital Malformations. Epidemiology of Human Congenital Malformations. Berlin, Germany: Springer, 2014:5-8.