Medical Journal of the
Islamic Republic of Iran

Volume 17
Number 4
Winter 1382
February 2004

# SCREENING OF FETAL CHROMOSOMAL ABNORMALITIES BY OBSTETRIC ULTRASONOGRAPHY IN TEHRAN, IRAN

**S.R. DADGAR, M.D.,* M.H. BADAKHSH, M.D.,* A. AMINI, M.D., ** AND SH. DADGAR, B.S.*****

*From the Department of Obstetrics and Gynecology, Iran University of Medical Sciences, Tehran, Islamic Republic of Iran.*

## ABSTRACT

Early identification of fetuses with chromosomal abnormalities enables health care providers to form an appropriate management plan for each patient. The main objective of this study was to determine the role of ultrasonography in screening and identifying fetuses at risk for chromosomal abnormalities.

A retrospective review of 6480 patients from the Obstetrics and Gynecology ward of Firouzgar hospital in Tehran was undertaken. Computer databases of patients were correlated to compare the results of the fetal ultrasonographic examination with the cytogenetic results from amniocentesis. Univariate and multivariate analyses were used to determine the best correlations between ultrasonography findings and chromosomal abnormalities.

Thirty-seven chromosomal abnormalities were found in 6480 fetuses (0.57%). Down syndrome was the most common finding with trisomy 18 and 13 being the next two most common abnormal findings. Multivariate analysis showed significant correlations between anomalies of the central nervous system, heart, face and neck, and extremities and increased nuchal fold, increased bowel echogenicity, abnormal biparietal diameter to femur ratio and the presence of chromosomal abnormalities ($p$ value<0.001).

Analysis of data indicated that the presence of any kind of ultrasonographic abnormality increases significantly the risk of fetal chromosomal abnormalities. It is also suggested that a normal ultrasonographic examination in an otherwise at-risk patient will significantly reduce the risk of fetal chromosomal abnormalities.

*MJIRI, Vol. 17, No. 4, 285-288, 2004.*

**Keywords:** Ultrasonography, Chromosomal abnormalities, Genetic amniocentesis and fetal anomalies.

## INTRODUCTION

Early identification of fetuses with chromosomal abnormalities enables health care providers to form an appropriate management plan for each patient. Screening for chromosomal abnormalities involves a careful patient and family history with appropriate referrals for genetic counseling, the use of biochemical screening tests and appropriate ultrasonographic studies.[1-3]

Chromosomal disorders occur in approximately 0.5% of newborns and it is well known its occurrence increases

*Assistant professor of Gynecology, Iran University of Medical Sciences.
**Associate professor of Gynecology, Iran University of Medical Sciences.
***B.S. in microbiology

with advancing maternal age.[4,5]

Chromosomal anomalies have been associated with abnormal ultrasonographic findings in 0.3% to 65% of cases depending on the types of ultrasonographic anomalies seen.[2]

Vintzileos et al. and others have reported a significant decrease in fetal aneuploidy in high-risk patients when a normal ultrasonographic examination is obtained.[6,7]

These findings have led some investigators to suggest that ultrasonography alone may be an alternative method of ruling out chromosomal abnormalities in patients who are reluctant to undergo amniocentesis.[8,9]

Although the controversy still continues, many physicians believe that it is appropriate to offer all patients the opportunity to undergo detailed second-trimester ultrasonographic examination in order to detect fetal anomalies.[10-19] The topic is complicated and needs medical facts and social, financial and ethical consideration.

The aim of this study is to clarify the role of ultrasonography in screening of fetal chromosomal abnormalities, in a retrospective study of patients who underwent genetic amniocentesis at Firouzgar hospital affiliated to Iran University of Medical Sciences.

## MATERIAL AND METHODS

This study was conducted in the obstetrics and gynecology ward of Firouzgar teaching hospital affiliated to Iran University of Medical Sciences in Tehran.

During a 48 - month period from September 1, 1998 to September 1, 2002, all women who referred to this center were enrolled. Of the 6710 patients who entered the study, the records of 230 patients were incomplete. Therefore the computer databases of 6480 patients from these wards were correlated to compare the results of the fetal ultrasonographic examination with the cytogenetic results from amniocentesis. The information obtained from this study was analyzed both with univariate and multivariate analysis to obtain the best correlation between ultrasonographic findings and amniocentesis results. The logistic regression was used for univariate and multivariate analysis. For all tests, a p value of $<0.05$ was considered significant.

## RESULTS

The mean maternal age at examination was 26.4 years (range, 18-35 years), and the mean gestational age at examination was 17.0 weeks (range 12.8-35.2 weeks). 81.2% of the patients scanned for the first time were between 14 and 18 weeks of gestation. There were 37 fetuses with chromosomal abnormalities (Table I) in this study group (0.57%). As expected, Down syndrome was the most common finding with trisomy 18 and 13 being the next two most common abnormal results.

**Table I.** Chromosomal abnormalities identified in Firouzgar hospital.

| Abnormality | No. of cases |
|---|---|
| Trisomy 21 | 24 |
| Trisomy 18 | 8 |
| Trisomy 13 | 4 |
| XXY | 1 |
| Total | 37(0.57%) |

### Univariate analysis

When no anomalies were seen and all long bone lengths and ratios were within normal limits, the incidence of chromosomal anomalies was 0.12%. As the number and severity of abnormal ultrasonographic findings increased, there was a rising in the incidence of chromosomal abnormalities. If no structural anomalies were seen but an abnormal bone length or ratio(s) was found the incidence of chromosomal anomalies increased to 1.05%. When only a single minor anomaly was seen, the incidence was 5.1%; when any major structural anomaly was seen the incidence increased to 35%. If two or more abnormal ultrasonographic findings of any type were seen, the incidence of fetal chromosomal abnormalities rose to 50%.

Table II shows the association between isolated ultrasonographic findings and the presence of fetal chromosomal abnormalities. Isolated anomalies of the spine, face, neck, heart or abdomen, increase in nuchal folds, bowel echogenicity and renal pyelectasis indicated significant associations with fetal chromosomal abnormalities by univariate analysis. There was no significant association with chromosomal anomalies of choroid plexus cyst(s), echogenic cardiac foci, short femur or abnormal biparietal diameter-to-femur length ratio.

### Multivariate analysis

The logistic regression analysis of findings indicated that only the following ultrasonographic findings provided the best prediction of the presence of a chromosomal abnormality: abnormality of the heart, or face and neck, increased nuchal folds, increased bowel echogenicity and abnormal biparietal diameter-to-femur length ratio. These results were used to construct regression to predict the presence or absence of chromosomal abnormalities on the basis of ultrasonographic findings.

For measuring equations, a value of 1 was used if a system anomaly was found by the ultrasonographic ex-

**Table II.** Incidence of fetal chromosomal abnormalities when only an isolated anomaly was seen on ultrasonographic evaluation.

| Findings | Chromosomal abnormalities (%) | Odds ratio and 95% confidence interval* |
|---|---|---|
| Spine | 35 | 240.1(16.5-7052) |
| Face or neck | 40 | 75.3(14-437.8) |
| Heart | 26 | 37.2(9.8-133) |
| Abdomen | 30 | 52.6(17.1-172.7) |
| Nuchal fold | 31 | 53.1(12.8-183.1) |
| Increased bowel echogenicity | 24 | 36.2(4.6-215) |
| Pyelectasis | 8 | 9.5(2.2-38.6) |
| Choroid plexus cysts | 2 | NS |
| Echogenic cardiac foci | 0 | NS |
| Short femur | 1 | NS |
| Biparietal diameter-to-femur length ratio | 3 | NS |

*Compared with negative findings (0.12)

**NS: not significant

**Table III.** Regression equation for prediction of fetal chromosomal abnormalities. (Normal= 0; abnormal= 1).

| Variable | Coefficient | Statistical significance |
|---|---|---|
| Constant | 0.02103 | $p<.0002$ |
| Biparietal diameter-to-femur length ratio | 0.03291 | $p< .0001$ |
| Central nervous system | 0.02898 | $p< .0002$ |
| Face and neck | 0.04039 | $p< .0001$ |
| Heart | 0.28902 | $p< .0001$ |
| Nuchal fold | 0.17112 | $p<.0001$ |
| Increased bowel echogenicity | 0.03024 | $p< .0001$ |

amination and a value of 0 if it was absent (Table III).

## DISCUSSION

The incidence of chromosomal abnormalities in this study was 0.57. Down syndrome was the most common finding, with trisomy 18 and 13 being the next two most common abnormal results. This study confirms the results of other investigators.[4,5]

The current study also is a report of the relationship between abnormal ultrasonographic findings and the presence or absence of fetal chromosomal anomalies in pregnant women. It confirms the strong association between structural abnormalities demonstrated on ultrasonographic examination and an increasing risk of fetal chromosomal abnormalities that has been reported by other investigators.[2]

In the presence of a single major structural anomaly, there was a 35% incidence of chromosomal abnormalities and the incidence increased to 50% when 3 or more major anomalies were found. In this study, the presence of one or more minor anomalies also increased the risk of chromosomal abnormalities. The significance of isolated minor findings on ultrasonographic examination are highly controversial. It is uncertain whether the presence of isolated choroid plexus cysts, increased echogenic foci in the heart or a single umbilical artery should be an indication for genetic aminocentesis.[12,16]

In the current study univariate analysis showed a strong association between increased nuchal folds, bowel echogenicity, renal pyelectasis, short humerus and abnormal femur length-to-abdominal circumference ratio and the presence of fetal chromosomal abnormalities; however, the same association was not shown with other systems.[17,19]

This study confirms the reports of Vintzeleos et al.[6] and others[2] who have suggested that a normal ultrasonographic examination in an otherwise at-risk patient will significantly reduce the risk of fetal chromosomal abnormalities. In the current study, there was a 2-to-3-fold decrease in the incidence of chromosomal abnormalities in fetuses that had completely normal ultrasonographic examinations. In the patients at high risk for chromosomal abnormalities, a normal ultrasonographic examination could be used to modify overall risk.[10,11] For the low risk obstetric population, additional studies are needed as there are a large number of patients at low risk of fetal chromosomal abnormalities.

## ACKNOWLEDGEMENTS

This project was supported by the Research Department of Iran University. Our appreciation goes to Dr Kholdebarin, the head of Firouzgar hospital for his support. We also thank our colleagues Dr Dadkhah; Dr Shabnam Dadgar; Dr Shafaghati; Dr Alavi; Dr Shirvani and Leila Ebrahimzadeh and many other colleagues for their support, efforts and patience.

## REFERENCES

1. Platt LD, Feutchbaum L, Filly R, et al: The California maternal serum alpha-fetoprotein-screening program: the role of ultrasonography in the detection of spina bifida. Am J Obstet Gynecol 166: 1328-9, 1992.
2. Ott WJ: The role of ultrasound in screening for chromosomal abnormalities. In: Ott WJ, (ed.), Clinical Obstetrical Ultrasound. New York: Wiley-Liss, pp. 333-52, 1999.
3. MacDonald ML, Wagner RM, Slotnick RN: Sensitivity and specificity of screening for Down syndrome with alpha-fetoprotein, HCG, and maternal age. Obstet Gynecol 77: 63-8, 1991.
4. Callen PW: Ultrasonography in obstetrics and gynecology. Philadelphia: W.B. Saunders Company, p. 20, 2000.
5. Evans MI, Hume RF, Johnson MP, et al: Integration of genetics and ultrasonography in prenatal diagnosis. Am J Obstet Gynecol 174: 1925, 1996.
6. Vintzileos AM, Campbell WA, Rodis J, Guzman ER, Smulain JC, Knuppel RA: The use of second trimester genetic sonogram in guiding clinical management of patients at increased risk for fetal trisomy 21. Obstet Gynecol 87: 948-52, 1996.
7. Nyberg DA, Luthy DA, Cheng EY, Sheley RC, Resta RG, Williams MA: Role of prenatal ultrasonography in women with positive screen for Down syndrome on the basis of maternal serum markers. Am J Obstet Gynecol 173: 1030-5, 1995.
8. Devore GR, Alfi O. The use of color Doppler ultrasound to identify fetuses at increased risk for trisomy 21: an alternative for high-risk patients who decline genetic amniocentesis. Obstet Gynecol 85: 378-86, 1995.
9. Nadel AS, Bromley B, Frigoletto FD, Benaserraf BR: Can the presumed risk of autosomal trisomy be decreased in fetuses of older women following a normal sonogram? Ultrasound Med 14: 297-302, 1995.
10. Botkin JR: Prenatal screening professional standards and the limits of prenatal choice. Obstet Gynecol 75: 875-80, 1990.
11. Druzin MI, Chervenack F, Mc Cullough LB, Blutman RN, Neidich JA: Should all pregnant patients be offered prenatal diagnosis regardless of age? Obstet Gynecol 81: 615-8, 1993.
12. OH WJ, Taysi K: Obstetric ultrasonographic findings and fetal chromosomal abnormalities. Am J Obstet Gynecol 7: 1414-1420, 2001.
13. Deren O, Mahoney MJ, Copel JA, Bahado-Singh R: Subtle ultrasonographic anomalies: do they improve the Down syndrome detection rate? Am J Obstet Gynecol 178: 441-5, 1998.
14. Vergani P, Locatelli A, Piccoli MG, Geruti EM, Pezullo JC, Ghidini A: Best second trimester sonographic markers for the detection of trimosy 21. J Ultrasound Med 18: 469-73, 1999.
15. Chitty LS, Chudlerigh P, Wricht E, Campbell S, Pembrey M: The significance of choroid plexus cysts in an unselected population: results of a multicenter study. Ultrasound Obstet Gynecol 12:301-7, 1998.
16. Mocos CL, Platt LD, Carlson DE, Gregory KD, Geene MH, Korst LM: The isolated choroid plexus cyst. Obstet Gynecol 92: 232-6, 1998.
17. Sepulveda W, Romero D: Significance of echogenic foci in the heart. Ultrasound Obstet Gynecol 12: 445-9, 1998.
18. Vibhakar NI, Bodorick NE, Scioscia AL, Harby LD, Mullen ML, Sklansky MS: Prevalence of aneuploidy with a cardiac intraventricular echogenic focus in an at-risk patient population. J Ultrasound Med 18: 265-8, 1999.
19. Chow JS, Benson C, Doubile PM: Frequency and nature of structural anomalies in fetuses with single umbilical arteries. J Ultrasound Med 17: 765-8, 1998.