in vivo *29*: 155-160 (2015)

Awareness of Prenatal Screening for Fetal Aneuploidy Among Pregnant Women in Greece

THOMAS KARAGKIOUZIS[1,2], STAVROS SIFAKIS[2], PERIKLIS MAKRITHANASIS[3], NICK DESSYPRIS[4], ELENI T. PETRIDOU[4], SOFIA KITSIOU-TZELI[1] and EMMANUEL KANAVAKIS[1]

[1]*Department of Medical Genetics, Medical School, Athens University, Athens, Greece;*
[2]*Department of Obstetrics-Gynecology, University Hospital of Heraklion, Heraklion, Greece;*
[3]*Department of Genetic Medicine and Development, Faculty of Medicine, University of Geneva, Geneva, Switzerland;*
[4]*Department of Hygiene, Epidemiology and Medical Statistics, Medical School, Athens University, Athens, Greece*

Abstract. *Aim: To estimate the level of awareness of prenatal screening (PS) and explore the underlying demographic, lifestyle and medical history parameters of Greek and non-Greek pregnant women undergoing prenatal diagnosis. Patients and Methods: A structured questionnaire was answered by 354 women at the time of receiving the results of invasive prenatal testing. Summary statistics and multiple logistic regression analyses were performed. Results: Adequate knowledge of the effectiveness of PS tests was reported by 50.8% of women. Popular press reading was associated with more than 2-fold higher level of awareness [odds ratio (OR)=0.51, p=0.0004]. Inadequate awareness was recorded among pregnant women of non-Greek nationality (OR=2.07, p=0.04), as well as among those also unaware of the effects of smoking during pregnancy (OR=2.39, p=0.004). Conclusion: Pre-gestational prenatal counseling is essential in order to improve knowledge and attitudes of women towards PS and reduce the health gap between different cultural and social groups.*

Prenatal diagnosis of fetal chromosomal abnormalities is based on invasive diagnostic tests (amniocentesis or chorionic villus samplings (CVS)] which allow for definite assessment and are used as a second line of study due to their invasiveness and relative risk for fetal loss. Non-invasive prenatal screening tests (PS) such as maternal serum biochemistry (Maternal Serum Screening, MSS) and Nuchal Translucency (NT) are routinely used as the first line for investigation (1-3).

Currently, many maternal serum biochemical marker schemes and ultrasonographic options are available but these tests can only estimate the risk of a pregnant woman carrying an affected fetus. Patients who screen positively are generally offered genetic counseling and definitive diagnosis through cytogenetic analysis of either CVS in the first trimester or amniotic fluid cells in the second trimester.

Acceptance of PS tests depends on the awareness of the public regarding the indications and benefits of these non-invasive procedures. Several studies have dealt with the attitudes, awareness and acceptability among women of childbearing age in various populations and geographical regions in Europe and elsewhere (4-24). In Greece, Mavrou *et al.* estimated the level of awareness and the use of available diagnostic services in a nationwide representative sample of 350 women with young children between the ages of 18-65 years (25). Another study was conducted in 2008 in order to examine whether the 135 pregnant women that had participated had made an informed choice concerning antenatal screening tests for Down syndrome (26). A dramatic increase in the number of economic refugees and immigrants into Greece has been reported (comprising approximately 10% of the population), which has altered the homogeneity of the population of pregnant women (27, 28).

The aim of the present study was to estimate the level of awareness of PS and explore the underlying demographic, lifestyle and medical history parameters of Greek and non-Greek pregnant women undergoing prenatal diagnosis. The study was conducted at the Department of Medical Genetics of Athens University, one of the two public medical genetics Centers in the region of Southern Greece, where prenatal chromosomal analysis of amniotic fluid cells or CVS is performed.

Correspondence to: Sofia Kitsiou-Tzeli, Department of Medical Genetics, Medical School, Athens University Choremio Research Laboratory, Aghia Sofia Children's Hospital, Athens 11527, Greece. Tel/Fax: +302107795553, e-mail: skitsiou@med.uoa.gr

Key Words: Prenatal screening, fetal aneuploidy, genetic counseling, awareness.

Patients and Methods

From August 2006 to October 2007, a total of 1018 pregnant women undergoing prenatal diagnosis using amniotic fluid samples or CVS were referred for chromosomal analysis. Since personal interviewing at the time of receiving the results and genetic counseling was not possible in all cases, only 354 pregnant women were included in the study. A total of 612 women were excluded because the results were given to their spouses or delivered by post, and in 52 cases communication was not possible due to language difficulties.

All eligible women were interviewed on the basis of a structured questionnaire eliciting information concerning sociodemographic, educational and lifestyle characteristics, family and personal medical history, as well as questions pertaining to the women's knowledge, use and opinion of PS. The questionnaire had been previously pilot tested and refined in a preliminary study of 30 respondents and the interviews lasted for approximately 30 minutes. Immigrants poorly speaking and understanding the Greek language were either interviewed in English or in their native language, if a translator was present. No women refused to be interviewed and informed consent was received from all the participants.

For statistical analysis, frequency distributions of the study variables among pregnant women who had "adequate" knowledge of PS and those with "inadequate" knowledge were generated and compared using the Chi-square test. Women with "adequate" knowledge were those aware of the purpose of the test and the possible chromosomal or other congenital anomalies of the fetus that could be revealed. The data were modelled through multiple logistic regression, using knowledge of prenatal testing ("adequate" *vs*. "inadequate") as the outcome variable in comparison to possible predictive variables such as age, education, nationality, marital status, reported family income status, knowledge of health consequences due to smoking, frequency of reading popular press, pre-existing knowledge of screening tests (Papanicolaou smear, mammography, fecal occult blood test), personal medical history (number of children, miscarriages, abortions, family history of inherited diseases), type of contact hospital (private or state) and source of existing information.

The SAS statistical package (SAS Institute Inc., NC, USA) was used in all analyses (accepted p-values <0.04).

Results

Based on the reply to the questionnaire regarding knowledge, use and opinion of PS, three out of ten women (28.8%) were not previously informed of the potential and effectiveness of PS. Despite the fact that 96.0% were directed to undergo prenatal testing by their physician (Table I), 188 (53.0%) women reported having no prior information on the implications of a 'normal' result of biochemical screening tests and another 192 (54.0%) reported so for ultrasonographic screening tests. Nevertheless, only 13.6% were dissatisfied with the information they had received. As far as their reaction in the case of a ''positive'' result of PS, 59.7% intended to ask their physician's opinion and another 34.7% would agree to further testing following the advice of their physician. Only 50.8% of the interviewed women had adequate awareness of the PS tests that they had already undertaken. Most of them, however, expressed their intention to undergo the same tests in a future pregnancy (96%).

The distribution of prenatal test awareness among 354 women based upon demographic and lifestyle variables, as well as prior knowledge of tests, other than prenatal screening tests, is presented in Table II. The data are mainly descriptive since they have not been mutually adjusted by the subsequent regression analysis. There are, however, indications that the variables related to a higher social profile were associated with better knowledge of PS. Specifically, better awareness of PS was observed among women of Greek origin with higher education, as well as among those with knowledge of the effects of smoking who were frequent readers of the popular press and had also prior knowledge of tests other than PS. An inverse association of PS awareness with the number of children was observed, whereas the number of miscarriages and abortions was not found to have a similar association. Women referred from private hospitals and those with a history of inherited diseases were better informed.

The results of the multiple logistic regression analysis are shown in Table III. Women of non-Greek origin were at a 2-fold risk of having inadequate awareness of PS as compared to Greek women [odds ratio (OR)=2.07, p=0.04]. Women who were unaware of the health consequences of smoking during pregnancy were also more likely to have inadequate knowledge of PS (OR=2.39, p=0.004), in contrast to those who reported reading the popular press (OR=0.51, p=10-4). Level of education, marital and family income status, knowledge of common screening tests, history of miscarriage and of inherited diseases did not reach nominal statistical significant (all p>0.05).

Discussion

Following changes in the strategies of PS during the past 15 years (30-33), as well as the influx of immigrants into Greece, this study was performed in order to determine women's awareness of non-invasive PS for fetal aneuploidy. It should be considered as the second part of a study among pregnant women undergoing prenatal diagnosis in Greece. The purpose of the first part performed using the same cohort was to estimate the knowledge and attitudes towards invasive prenatal procedures such as amniocentesis and CVS (29).

In the present study, testing women's awareness of non-invasive PS tests, it was shown that the number of pregnant women with adequate knowledge of PS was only slightly increased as compared to a previous study in Greece (50.8% *vs*. 45%) (26). Interestingly, most pregnant women declared their satisfaction with the information they had received and the majority (95.2%) expressed their willingness to repeat

Table I. *Distribution of 354 women by knowledge (K), use (U) and opinion (O) variables regarding prenatal screening (PS) tests.*

Variable	N (%)
Source of existing information (invasive/non-invasive procedures) (K):	
No information	102 (28.8)
Friends-TV-press	155 (43.8)
Previous medical history	69 (19.5)
Health related profession	28 (7.9)
Recommendation for the current PS test made by (U):	
Physician only	340 (96.0)
Physician and own positive attitude	14 (4.0)
Perceived level of information provided in case of a 'normal' test result by MSS (K)	
No information/incorrect interpretation	188 (53.0)
Adequate	166 (47.0)
Perceived level of information provided in case of a 'normal' test result of NT (K)	
No information/incorrect interpretation	192 (54.0)
Adequate	162 (46.0)
Reaction in case of 'positive' result of PS tests (NT/MSS)	
Ask the physician	211 (59.7)
Ask the physician and perform further examination	123 (34.7)
Termination of pregnancy	4 (1.1)
Undecided	16 (4.5)
Satisfied with the information provided upon receiving the results of the test (O)	
Yes	25 (7.1)
Partially	281 (79.3)
Displeased	34 (9.6)
No information given	14 (4.0)
PS tests should be used by all pregnant women (O)	
Yes, by all (to all pregnant women)	337 (95.2)
No	17 (4.8)
Attitude towards undergoing PS tests in next pregnancy (U)	
Positive, would undergo PS	337 (95.2)
Adequate knowledge about PS tests (K)	
Yes	180 (50.8)

MSS: Maternal serum screening; NT: nuchal translucency.

the same test in a future pregnancy, a fact that indicates the accessibility and acceptance of the PS tests by the public. A similar trend was previously noted in related studies that took place in Helsinki, Finland and in Picardi, France (5, 6).

As expected, the logistic regression analysis showed that Greek pregnant women were better informed about PS than immigrants (Table III). This fact has an important impact on public health as the number of immigrants of reproductive age in Greece progressively increases. Nevertheless, this study is subject to geographical and other limitations and it is currently unknown whether the proportion of immigrants who participated in the current study (approximately 25%) represents the true proportion of this subgroup in the overall reproductive population.

Statistical analysis also revealed that women reading popular press and aware of smoking consequences during pregnancy had better knowledge of the potential power and limitations of PS. Although the level of education, marital status and family income did not reach statistical significance in our study, it seems that women of lower social profile are at a higher risk of being unaware of the role of PS. This study therefore confirms the importance of nationality and socioeconomic status as predictors of adequate awareness of PS and is in agreement with previous studies (1, 9, 12, 19-21, 23, 24). Importantly, our findings confirm observations in various populations that women from minority ethnic groups and with low socioeconomic status do not have negative attitudes towards genetic testing, but rather have lower rates of informed choice (15, 22).

Overall, the present results are in agreement with previous international studies about the importance of information availability regarding antenatal non-invasive screening procedures (1, 12, 15, 25, 26, 34-36). What differentiates the present study from others is that women were interviewed upon receiving the results of the prenatal invasive testing and had recently been informed by their physicians or other sources. To our knowledge, the latter issue has not been previously investigated and emphasizes the significance of

Table II. *Distribution of prenatal screening awareness among 354 women by demographic and lifestyle variables, as well as prior knowledge about other screening tests.*

Variable	Knowledge				*p*-Value
	No		Yes		
	N	%	N	%	
Age					0.18*
<35 years	21	12.1	29	16.1	
35-36	42	24.1	50	27.8	
37-38	62	35.6	53	29.5	
39-40	26	15.0	31	17.2	
41+	23	13.2	17	9.4	
Education					0.001*
<7	16	9.2	7	3.9	
7-9	27	15.5	14	7.8	
10-12	85	48.8	58	32.2	
13-15	17	9.8	37	20.6	
16+	29	16.7	64	35.5	
Nationality					0.001*
Greek	105	60.3	160	88.9	
Other	69	39.7	20	11.1	
Marital Status					0.95*
Married	166	95.4	172	95.6	
Other	8	4.6	8	4.4	
Reported family income status**					0.001*
Poor	56	32.2	20	11.1	
Adequate	98	56.3	111	61.7	
Affluent	20	11.5	49	27.2	
Knowledge of health consequences due to smoking					0.001*
Yes	38	21.8	116	64.4	
No	136	78.2	64	35.6	
Frequency of lay press reading					0.001*
Never	106	60.9	33	18.3	
Rare	50	28.7	62	34.4	
1-2 times per month	16	9.2	63	35.0	
Weekly	2	1.2	22	12.2	
Preexisting knowledge of other screening tests					0.001*
0 tests	10	5.8	0	0.0	
1	3	1.7	1	0.6	
2	158	90.8	156	86.6	
3	3	1.7	23	12.8	
Children alive					0.03*
0	41	23.6	47	26.1	
1	75	43.1	94	52.2	
2	41	23.6	32	17.8	
3+	17	9.7	7	3.9	
Miscarriages					0.63*
0	134	77.0	131	72.8	
1	29	16.7	40	22.2	
2+	11	6.3	9	5.0	
Abortions					0.04*
0	111	63.8	127	70.6	
1	30	17.2	36	20.0	
2+	33	19.0	17	9.4	
Type of contact hospital					0.05*
State	168	96.6	165	91.7	
Private	6	3.4	15	8.3	
Family history of inherited diseases					0.03*
Yes	29	16.7	47	26.1	
No	145	83.3	133	73.9	

*Chi-square test with 1 degree of freedom. **As evaluated and stated by each subject.

Table III. *Logistic regression-derived odds ratios (ORs) and 95% confidence intervals (95% CIs) for prenatal screening awareness based on demographic, lifestyle and medical history predictors.*

Variable	Category or increment	OR	95% CI	*p*-Value
Age	2 More years	1.19	0.94-1.51	0.15
Education	3 More years	0.84	0.64-1.09	0.18
Nationality	Greek	Reference	1.05-4.09	0.04
	Other	2.07		
Marital status	Married	Reference	0.20-2.53	0.60
	Other	0.71		
Reported family income status	One more category	1.15	0.73-1.81	0.55
Knowledge of health consequences due to smoking	Yes	Reference	1.33-4.30	0.004
	No	2.39		
Frequency of lay press reading	One more category	0.51	0.35-0.74	0.0004
Pre-existing knowledge of screening tests	One more test	0.49	0.18-1.32	0.16
Children	>1	1.17	0.83-1.65	0.36
Miscarriages	>1	0.79	0.50-1.25	0.32
Abortions	>1	1.27	0.88-1.82	0.21
Type of contact hospital	Public	Reference	0.18-2.67	0.34
	Private	0.57		
Family history of inherited diseases	Yes	Reference	0.74-5.69	0.30
	No	1.41		

our findings. A limitation of the present study is that the interviewed population comprised pregnant women who were referred to the Department of Medical Genetics, and is probably not representative of the total Greek population as by the National Statistical Service of Greece (27). It is not feasible for this population to be compared with the number of women undergoing prenatal chromosomal analysis in the country as a whole, due to the lack of a nationwide systematic registry. Furthermore, it is not known how many prenatal samples are analyzed in private *vs*. state laboratories. As the proportion of samples from immigrants may be different at private centers, this might have an unavoidable influence on our findings. However, it should be noted that the Department of Medical Genetics currently covers the main workload of the increasing demand for state prenatal testing in Athens, southern Greece, as well as the island population.

In conclusion, the study identifies a specific group of immigrant pregnant women in Greece with inadequate awareness regarding the currently available PS procedures which should be targeted for pre-gestational counseling by healthcare professionals in the field. Immigrant women, as well as women with low socioeconomic status, require extended time for discussion and information given should be more intelligible. This is also of prime importance for all European Union countries experiencing an influx of immigrants of reproductive age. To reduce the health gap between cultural and social groups, specific interventions need to be developed and evaluated for their effectiveness at increasing the consistency of attitudes and knowledge. Such interventions are likely to be relevant in reducing social and cultural inequalities, not only regarding non-invasive PS, but also other screening programs and, more broadly, other healthcare provisions.

References

1 Rostant K, Steed L and O'Leary P: Survey of the knowledge, attitudes and experiences of Western Australian women in relation to prenatal screening and diagnostic procedures. Aust N Z J Obstet Gynaecol *43*: 134-138, 2003.

2 Nicolaides KH: First-trimester screening for chromosomal abnormalities. Semin Perinatol *29*: 190-194, 2005.

3 Norton M: Genetic screening and counseling. Curr Opin Obstet Gynecol *20*: 157-163, 2008.

4 Browner C, Preloran H and Press N: The effects of ethnicity, education and an information video on pregnant women's knowledge and decisions about a prenatal diagnostic screening tests. Patiend Educ Couns *27*: 135-146, 1996.

5 Salonen R, Kurki L and Lappalainen M: Experiences of mothers participating in maternal serum screening for Down's syndrome. Eur J Hum Genet *4*: 113-119, 1996.

6 Gekas J, Gondry J, Mazur S, Cesbron P and Thepot F: Informed consent to serum screening for Down syndrome: Are women given adequate information? Prenat Diagn *19*: 1-7, 1999.

7 Michie S, Smith D and Marteau T: Prenatal tests: How are women deciding? Prenat Diagn *19*: 743-748, 1999.

8 De Vigan C, Vodovar V, Coujard J, Garel M, Vayssiere C and Goffinet F: Mothers' knowledge of screening for trisomy 21 in 1999: a survey in Paris maternity units. Eur J Obstet Gynecol Reprod Biol *104*: 14-20, 2002.

9 Chilaka V, Konje J, Stewart C, Narayan H and Taylor D: Knowledge of Down syndrome in pregnant women from different ethnic groups. Prenat Diagn *21*: 159-164, 2001.

10 Al-Jader L. Parry-Langton N and William Smith RJ: Survey of attitudes of pregnant women towards Down syndrome screening. Prenat Diagn *20*: 23-29, 2000.
11 de Graaf IM, Tijmstra T, Blecker OP and van Lith JMM: Women's preference in Down syndrome screening. Prenat Diagn *22*: 624-629, 2002.
12 Suriadi C, Jovanovska M and Quinlivan JA: Factors affecting mothers' knowledge of genetic screening. Aust NZ J Obstet Gynaecol *44*: 30-34, 2004.
13 Michie S, Dormandy E and Marteau TM: Increasing screening uptake amongst those intending to be screened: the use of action plans. Patiend Educ Couns *55*: 218-222, 2004.
14 Van den Berg M, Timmermans DR, Ten Kate LP, van Vugt JM and van der Wal G: Are pregnant women making informed choices about prenatal screening? Genet Med *7*: 332-338, 2005.
15 Dormandy E, Michie S, Hooper R and Marteau TM: Low uptake of prenatal screening for Down syndrome in minority ethnic groups and socially deprived groups: A reflection of women's attitudes or a failure to facilitate informed choices? Int J Epidemiol *34*: 346-352, 2005.
16 Knoshnood B, de Vigan C, Blondel B, Lhomme A, Vodovar V, Garel M and Goffinet F: Women's interpretation of an abnormal result on measurement of fetal nuchal translucency and maternal serum screening for prenatal testing of Down syndrome. Ultrasound Obstet Gynecol *28*: 242-248, 2006.
17 Müller MA, Bleker OP, Bonsel GJ and Bilardo CM: Women's opinions on the offer and use of nuchal translucency screening for Down syndrome. Prenat Diagn *26*: 105-111, 2006.
18 Li DK, Karlberg K, Wi S and Norem C: Factors influencing women's acceptance of prenatal screening tests. Prenat Diagn *28*: 1136-1143, 2008.
19 Alderdice F, McNeill J, Rowe R, Martin D and Dornan J: Inequalities in the reported offer and uptake of antenatal screening. Public Health *122*: 42-52, 2008.
20 Fransen MP, Wildschut HI, Vogel I, Mackenbach JP, Steegers EA and Essink-Bot ML: Ethnic differences in considerations whether or not to participate in prenatal screening for Down syndrome. Prenat Diagn *29*: 1262-1269, 2009.
21 Fransen MP, Wildschut HI, Vogel I, Mackenbach J, Steegers E and Essink-Bot ML: Information about prenatal screening for Down syndrome: ethnic differences in knowledge. Patient Educ Couns *77*: 279-88, 2009.
22 Fransen MP, Essink-Bot ML, Vogel I, Mackenbach JP, Steegers EA and Wildschut HI: Ethnic differences in informed decision-making about prenatal screening for Down's syndrome. J Epidemiol Community Health *64*: 262-268, 2010.
23 Yanikkerem E, Ay S, Ciftçi AY, Ustgorul S and Goker A: A survey of the awareness, use and attitudes of women towards Down syndrome screening. J Clin Nurs *22*: 1748-1758, 2013.
24 Kosec V, Zec I, Tislarić-Medenjak D, Kuna K, Simundić AM, Lajtman-Krizaić M, Lovrić B, Mimica M, Estatiev ZK and Borgudan V: Pregnant women's knowledge and attitudes to prenatal screening for fetal chromosomal abnormalities: Croatian multicentric survey. Coll Antropol *37*: 483-489, 2013.
25 Mavrou A, Metaxotou C and Trichopoulos D: Awareness and use of prenatal diagnosis among Greek women: a national survey. Prenat Diagn *18*: 349-355, 1998.
26 Gourounti K and Sandal J: Do pregnant women in Greece make informed choices about antenatal screening for Down's syndrome? A questionnaire survey. Midwifery *24*: 153-162, 2008.
27 National Demographic Characteristics of the Greek Population. www.statistics.gr (last accessed 15 March 2006), 2006.
28 Eurostat. Demographic statistics: Total fertility rate - number of children per woman. 2006. http://epp.eurostat.ec.europa.eu/tgm/table.do?tab=table&init=1&language=en&pcode=tsdde220&plugin=1.
29 Kitsiou-Tzeli S, Petridou ET, Karagkiouzis T, Dessypris N, Makrithanasis P, Sifakis S and Kanavakis E: Knowledge and attitudes towards prenatal diagnostic procedures among pregnant women in Greece. Fetal Diagn Ther *27*: 149-155, 2010.
30 Kotz D: Screening for all. New guidelines urge every pregnant woman to get early testing for risk of Down syndrome. US News World Rep *142*: 78, 2007.
31 Driscoll DA, Morgan MA and Schulkin J: Screening for Down syndrome: changing practice of obstetricians. Am J Obstet Gynecol *200*: 459.e1-9, 2009.
32 Soler A, Morales C, Badenas C, Rodríguez-Revenga L, Carrió A, Margarit E, Costa D, Borrell A, Goncé A, Milà M and Sánchez A: A retrospective and theoretical evaluation of rapid methods for detecting chromosome abnormalities and their implications on genetic counseling based on a series of 3868 CVS diagnoses. Fetal Diagn Ther *23*: 126-131, 2008.
33 Christopoulou S, Christopoulou G, Hatzaki A, Hatzipouliou A, Donoghue J, Karkaletsi M, Kaminopetros P, Sifakis S and Velissariou V: The replacement of cytogenetic analysis by direct chorionic villi sampling preparation with quantitative fluorescence PCR. Gynecol Obstet Invest *68*: 255-261, 2009.
34 National Screening Committee: National Screening Committee, Second Report of the UK National Screening Committee. Department of Health, London, 2000.
35 National Screening Committee: National Screening Committee, Antenatal Screening for Down's Syndrome: Policy and Quality Issues. Department of Health, London, 2003.
36 RCOG: Royal College of Obstetrician and Gynecologists, Guidelines for Antenatal Care, Routine Care for Healthy Pregnant Women. RCOG: London, 2003.

Received October 29, 2014
Revised November 7, 2014
Accepted November 10, 2014