



## ARAŞTIRMA / RESEARCH

# Role of affective temperaments on decision-making processes of preferring invasive karyotype tests

Mizaç özelliklerinin invaziv karyotip testlerini seçme kararları üzerine olan etkisi

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*Cukurova Medical Journal 2021;46(4):1387-1393*

### Abstract

**Purpose:** The aim of this study was to evaluate the relationship between patient temperament and preference for invasive prenatal tests.

**Materials and Methods:** This was a prospective study of 337 pregnant women who had increased risk of having a fetus with Down syndrome. Their temperament profile was determined by using the temperament evaluation of TEMPS-A. Women were grouped as accepting (study) or declining (control) to perform an invasive test.

**Results:** 284 pregnancies were included in the final analyzes. The study group had more likely employed and had a higher level of education level. There was no predominant temperament in 247 (87%) women. Hyperthymic temperament had the highest scores ( $11.2 \pm 4.1$ ) among other four temperament types. Study group patients had lower scores for anxious and depressive temperaments compared with control groups.

**Conclusion:** Women who had a less anxious or depressive personality were more likely to prefer an invasive prenatal test. In addition, employment and higher educational status were correlated with undergoing invasive prenatal testing.

**Keywords:** Affective temperament, anxious, depressive, invasive tests, amniocentesis

### Öz

**Amaç:** Bu çalışmanın amacı gebelerin mizaç özellikleri ile invaziv testi tercih etmeleri arasındaki ilişkinin değerlendirilmesi amaçlanmıştır.

**Gereç ve Yöntem:** Mevcut çalışma fetüste Down sendromu açısından artmış riske sahip 337 gebeliğin prospektif değerlendirilmesini içermektedir. Hastaların mizaç özellikleri TEMPS-A skalası aracılığıyla belirlenmeye çalışılmıştır. Gebeler invaziv test yapılmasını kabul edenler (çalışma) ve etmeyenler (kontrol) şeklinde iki gruba ayrılmıştır.

**Bulgular:** Nihai analizler 284 gebe üzerinden yapılmıştır. Çalışma grubundaki hastalarda düzenli bir işte çalışma oranı ve eğitim seviyesi kontrol grubuna göre daha yüksek bulunmuştur. Hastaların 247'sinde (%87) baskın bir mizaç saptanmadı. Bununla birlikte en yüksek skor hipertimik mizaca ( $11.2 \pm 4.1$ ) ait olarak bulundu. Çalışma grubundaki hastalar daha düşük anksiyetik (ve depresif (mizaç skorlarına sahiplerdi).

**Sonuç:** Daha düşük anksiyöz ya da depresif mizaç özelliklerine sahip hastalar invaziv tanı testlerini daha yüksek oranda tercih etmektedirler. Buna ek olarak düzenli bir işte çalışma ve daha yüksek eğitim durumu da invaziv prenatal testi yaptırmayla ilişkilidir.

**Anahtar kelimeler:** Mizaç, anksiyöz, depresif, invaziv testler, amniyosentez

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Geliş tarihi/Received:03.08.2021 Kabul tarihi/Accepted: 15.09.2021 Çevrimiçi yayın/Published online: 17.09:2021

## INTRODUCTION

Down syndrome is the most common genetic disorder with a prevalence of 1 in every 700 live births<sup>1</sup>. Therefore, it is a common goal of perinatal medicine to identify the pregnancies having a fetus with Down syndrome. For determining high risk pregnancies, first and second trimester screening tests are the two most common screening tests in Turkey<sup>2</sup>. In addition advanced maternal age, history of a previous pregnancy that resulted with chromosomal disorder, and several sonographic signs are used to predict an increased risk of having a fetus with Down syndrome, each with different predictive rates<sup>3</sup>.

These screening tools have been used to separate high risk pregnancies from low risk pregnancies and to identify the candidates for diagnostic tests. Invasive tests such as chorionic villus sampling (CVS), and amniocentesis are used for definitive diagnosis. Currently, these tests have an up to 1% risk of fetal loss<sup>4</sup> which affects a patient's decision for undergoing the test<sup>5</sup>. Several factors such as knowledge about Down syndrome and religious/ethical beliefs have been investigated in how they impact patient preferences for invasive prenatal testing<sup>4,6,7</sup>. No studies has evaluated the relationship between personal affective temperaments and decisions to undergo invasive prenatal tests.

In this study we investigated the role of patients' affective temperaments on the decision making process for invasive prenatal procedures. Our secondary aim was to evaluate if any other demographic or pregnancy factors were associated with patients' willingness to undergo diagnostic tests.

## MATERIALS AND METHODS

This was a prospective case-control study of 337 pregnancies who applied to Division of Maternal Fetal Medicine at Cukurova University School of Medicine for counseling about prenatal diagnostic tests because of having a fetus with increased risk of trisomy 21. Pregnancies between 11 to 22 gestational weeks, that had increased risk for trisomy 21, such as having advanced maternal age over 35 years old, a history of pregnancy with chromosomally abnormal fetus, positive screening in first and second trimester screening tests, or "soft" markers of trisomy 21 detected by second trimester ultrasound screening (such as having a nuchal fold thickness >6 mm, nasal bone shorter than 5% percentile, or having aberrant

right subclavian artery etc.)<sup>8</sup> were included. Excluded patients were pregnancies with a major anomaly (e.g., omphalocele), in addition to positive screening tests or "soft" markers, prior non-invasive prenatal testing (NIPT), previously diagnosed with any psychiatric disease or other medical conditions, multiple pregnancies, <18 years of age or who did not understand Turkish clearly. Likewise patients who did not complete the temperament questionnaire, and had no medical indications for invasive testing but preferred it due to maternal anxiety were excluded too. Of those 337 patients, 284 patients were included the study while remaining 53 patients were excluded where 18 did not complete questionnaire, 17 had major fetal anomalies, 6 preferred invasive testing due to maternal anxiety without any medical indications, 4 had NIPT, 3 had multiple pregnancies, 3 had major depression and one had bipolar disorder, and 1 was <18 years old.

Informed consent form was signed by all participants and study was approved by local ethic committee of Cukurova University School of Medicine (No: 75/76-13.04.2018) and the research complied with Declaration of Helsinki<sup>14</sup>.

## Procedure

Before participation, detailed information about the study was given and informed consent was obtained from all patients. Patients were told that refusing to participation in the study would not make any difference in their medical treatment. Sociodemographic (maternal age, education status, employment status) and pregnancy (gravity, parity, history of previous miscarriage) characteristics of patients, and indication for invasive testing were recorded.

Indications were classified as 1) "increased risk due history" that included patients who had advanced maternal age that did not undergo screening test but instead chose invasive test or refused both of them as well patients with a positive history of pregnancy resulted with chromosomal abnormality, 2) "having positive screening test" that included a higher risk of trisomy 21 over 1/100 in first or second trimester screening, and 3) "soft markers" including minor signs during second trimester ultrasound screening<sup>9,10</sup>

## Measures

Participants were asked to complete temperament evaluation of Memphis, Pisa, Paris and San Diego –

autoquestionnaire (TEMPS-A). Temperament of pregnant women was measured by using Turkish version of the TEMPS-A Scale, which was designed by Akiskal et al. in 1997 and was translated and validated for Turkish participants by Vahip et al. in 2005<sup>11,12</sup>. Affective temperaments were diagnosed by 99 questions (20 questions were related with hyperthymic temperament, 20 with cyclothymic, 17 with irritable, 23 with anxious and the remaining 19 with depressive temperament) with answers of true/false considering the patient's entire life period. Patients were separated into two groups. The first group (study group) consisted of patients who underwent invasive testing. The second group (control group) consisted from those refusing to have the invasive testing. No patients chose the NIPT which has been shown to identify the trisomy 21 with a more than 99% accuracy<sup>13</sup>.

### Statistical analysis

Statistical analysis of the study was processed using the Statistical Package for the Social Sciences Version 22.0 (IBM Corp., NY, USA). Continuous variables were evaluated by t-test. Categorical variables were analyzed with Mann-Whitney U test or Pearson's chi-square test where available. Correlations between variables were evaluated by Pearson correlation test. Univariate and multivariate regression analysis were performed to find the relationship between clinical

factors and invasive test preference.  $p < 0.05$  was considered statistically significant.

### RESULTS

Of those 284 patients, 181 (63.7%) underwent invasive testing while 103 (36.3%) declined to have invasive test. Of the 181 patients who accepted invasive tests, 51 (28%) underwent CVS and 130 (72%) underwent amniocentesis. The mean maternal age was  $32.1 \pm 6.4$  and the mean gestational week was  $17.1 \pm 3.1$ . Sixty-two women (22%) were nulliparous, and 204 (72%) had no history of abortion. Only 88 (31%) patients were employed and the remaining 196 (69%) were housewives. Of those 80 women (28%) had an education of  $\leq 5$  years, 52 (18%) had 5-8 years, 70 (25%) had 8-11 years and the remaining 82 (29%) had  $>11$  years of education, respectively. While the mean maternal age, parity and abort history were not different between two groups, the study group had a higher level of education status and was more likely employed (Table 1).

The most common invasive test indication was positive screening test with a number of 199 (70%) and following by soft markers in 54 (19%) women and increased risk due history in 31 (11%) women, respectively. But there was no significant difference in invasive test indications between two groups (Table 2)..

**Table 1. Sociodemographic and pregnancy characteristics of patients.**

	Study group (n=181)	Control group (n=103)	p value
Maternal age (years)	$32.3 \pm 6.3$	$31.7 \pm 6.7$	NS
Gestational age (weeks)	$17.9 \pm 2.9$	$16.6 \pm 3.1$	0.001
Parity			NS
Nulliparous	43 (24%)	19 (17%)	
Multiparous	138 (76%)	84 (83%)	
Abort history			NS
Yes	52 (29%)	28 (27%)	
No	129 (71%)	75 (73%)	
Education level (years)			0.001
$\leq 5$	39 (21%)	41 (40%)	
5-8	30 (17%)	22 (21%)	
8-11	49 (27%)	21 (20%)	
$\geq 11$	63 (35%)	19 (19%)	
Employment status			<0.05
Employed	64 (35%)	24 (23%)	
Non-employed	117 (65%)	79 (77%)	

NS: Non-significant

**Table 2. Invasive test indications due to groups**

	Study group (n=181)	Control group (n=103)	p value
Invasive test indications			NS
Increased risk due history	25 (14%)	6 (6%)	
Positive screening test	121 (67%)	78 (76%)	
Soft markers	35 (19%)	19 (18%)	

NS: Non-significant

**Table 3. Temperament comparison between patients**

	Study group (n=181)	Control group (n=103)	p value
Depressive	5.3 ± 3.6	6.9 ± 5.4	< 0.05
Cyclothymic	7.4 ± 5.0	8.3 ± 4.7	NS
Hyperthymic	11.1 ± 4.3	11.2 ± 3.6	NS
Irritable	3.5 ± 3.3	3.6 ± 4.2	NS
Anxious	6.6 ± 5.6	8.3 ± 6.1	< 0.05

NS: Non-significant

**Table 4. Correlation between depressive and anxious temperament and other clinical factors**

	Depressive Temperament	Anxious Temperament
Maternal age		
Pearson correlation	.007	-.094
Sig. (2-tailed)	.902	.118
Gestational age		
Pearson correlation	.106	-.006
Sig. (2-tailed)	.074	.923
Parity		
Pearson correlation	.112	.103
Sig. (2-tailed)	.065	.092
Abort history		
Pearson correlation	.134	.044
Sig. (2-tailed)	.028	.470
Indications		
Pearson correlation	-.006	-.050
Sig. (2-tailed)	.924	.397
Employment status		
Pearson correlation	-.209	-.163
Sig. (2-tailed)	.000	.006

**Table 5. The association between preference of invasive prenatal tests and clinical factors**

	Univariate OR (95% CI)	Univariate P-value	Multivariate OR (95% CI)	Multivariate P-value
Parity	0.676 (0.360, 1.268)	0.2	1.218 (0.595, 2.494)	0.6
History of abortus	0.751 (0.627, 1.910)	0.8		
Education				
≤5 years	0.287 (0.146, 0.563)	0.0001	0.351 (0.148, 0.832)	0.017
5-8 years	0.411 (0.194, 0.873)	0.02	0.479 (0.185, 1.242)	0.1
8-11 years	0.704 (0.341, 1.452)	0.3	0.9 (0.38, 2.131)	0.8
>11 years	Reference		Reference	
Employment status	1.801 (1.040, 3.118)	0.04	1.020 (0.48, 2.169)	0.958
Depressive	0.914 (0.858, 0.974)	0.006	0.944 (0.866, 1.03)	0.2
Cyclothymic	0.963 (0.917, 1.011)	0.1	1.042 (0.965, 1.125)	0.3
Hyperthymic	0.995 (0.937, 1.056)	0.865	1.065 (0.977, 1.148)	0.5
Irritable	0.991 (0.93, 1.055)	0.774	1.054 (0.971, 1.142)	0.4
Anxious	0.953 (0.914, 0.993)	0.021	0.969 (0.909, 1.034)	0.3

Of those 284 patients, 247 (87%) of them did not have any affective temperament and only 37 had at least one affective temperament. Nearly half of (n=17) the patients who had an affective temperament had more than one and the most common affective temperament was anxious (n=22) followed by depressive (n=17) temperament.

The highest scores for the type of temperaments belonged to hyperthymic ( $11.2 \pm 4.1$ ) followed by cylothymic ( $7.7 \pm 4.9$ ), anxious ( $7.3 \pm 5.8$ ), depressive ( $5.9 \pm 4.4$ ) and irritable ( $3.5 \pm 3.8$ ) temperaments. Depressive ( $5.3 \pm 3.6$  vs.  $6.9 \pm 5.4$ ,  $p < 0.05$ ) and anxious ( $6.6 \pm 5.6$  vs.  $8.3 \pm 6.1$ ,  $p < 0.05$ ) temperaments had lower scores in the study group compared with the control group (Table 3)

Furthermore, we investigated if depressive and anxious temperaments were correlated with any other factors. We found that depressive temperament was positively associated with abort history ( $r = 0.134$ ,  $p < 0.05$ ) and negatively associated with education level ( $r = -0.285$ ,  $p < 0.001$ ), and employment status ( $r = 0.209$ ,  $p < 0.001$ ). Likewise anxious temperament was negatively associated with education level ( $r = -0.216$ ,  $p < 0.001$ ) and employment status ( $r = -0.163$ ,  $p < 0.01$ ) (Table 4).

In univariate regression analysis  $\leq 5$  years (Odds ratio [OR] 0.29, 95% confidence intervals [CI] 0.15-0.56,  $p = 0.0001$ ) and 5-8 years education (OR 0.41, 95% CI 0.19-0.87,  $p = 0.02$ ), depressive temperament (OR 0.91, 95% CI 0.86-0.97,  $p = 0.006$ ), anxious temperament (OR 0.95, 95% CI 0.91-0.99,  $p = 0.02$ ) and employment (OR 1.80, 95% CI 1.04-3.11,  $p = 0.04$ ) were associated invasive prenatal test preference. However on multivariate analysis only  $\leq 5$  years education (OR 0.35, 95% CI 0.15-0.83,  $p = 0.01$ ) was found to be associated factor (Table 5)

## DISCUSSION

This study evaluated the effect of temperament characteristics of pregnant women on preferring invasive prenatal testing in the setting of having an increased risk for a fetus with trisomy 21. This study revealed that women that were less educated and less employed as well those had higher scores of depressive and anxious temperaments, less frequently preferred invasive prenatal tests.

Pregnancy is mostly known as a period of mental quietness, frequently related with specific hormonal

fluctuations during this period<sup>15</sup>. Various studies have shown that hyperthymic temperament was more significant during the perinatal period than the other types<sup>11,16</sup>. In parallel to these findings, the scores of hyperthymic features in our study were higher than the other temperament types in all patients as well in the subgroups. Depressive or anxious temperaments scores were higher compared with previous studies<sup>16,17</sup>. This might arise from the different characteristics of study populations. Prior studies evaluated pregnancies from general population whereas our study population had a higher mean maternal age. In addition, some of the women in our study had prior children with Down syndrome which may have affected their psychological status.

Having a fetus with Down syndrome is one of the most stressful thoughts for women during pregnancy. Several screening tests exist for determining high risk pregnancies. While there is a chance for certain diagnosis by prenatal invasive tests, it is still a complicated process for most of families since the invasive tests have risk of pregnancy loss. Similarly, trisomy 21 is not a treatable condition and the only option is pregnancy termination<sup>6,18,19</sup>. But decision of termination of pregnancy is based on several factors such as patients' attitudes and religious beliefs towards termination, and socioeconomical factors<sup>6,7</sup>. And even in developed European countries like Germany recent data showed that nearly 1/3 of families continued their pregnancies despite the fetus was diagnosed with Down syndrome<sup>20</sup>. And 28% of the continued ones did not perform karyotype analysis because they had already decided not to terminate their pregnancy even the Down syndrome would be diagnosed. Another study showed that two major reasons for women refusing the invasive tests were that the results would not impact a plan to continue a pregnancy and that women feared with the risk of losing a healthy pregnancy<sup>5</sup>.

While 36% of patients declined the invasive tests in our study, we did not have information about their reasons. Similarly to previous studies, we found that patients who underwent invasive diagnostic tests were more likely employed and had higher level of education comparing the control group<sup>6</sup>. The more the women are educated, the more they comprehend the circumstances of the disease or a child with Down syndrome and this might be an important factor on decision-making processes. Likewise employed women more likely chose the invasive tests since a child with Down syndrome would need more care,

time and energy spent by parents<sup>21</sup>. However it would be hard for a working mother to sufficiently take care of an unhealthy child.

Of the 5 types of temperaments, depressive and anxious types had significantly higher scores in patients declining the invasive testing. The higher anxious temperament scores might be related with the fear of loosing a healthy baby due to invasive test<sup>5,22</sup>. Likewise as patients with depressive personality more likely focused on the worse aspects they might think that they would loose pregnancy if they had invasive test<sup>23</sup>. Moreover, patients with depressive personality have difficulties to make decisions and are more likely to procrastinate the decisions<sup>24</sup>. These temperaments were negatively correlated with education and employment status, which can be another explanation for less choosing the diagnostic test.

This study was the first study in the literature to investigate the role of a patient's temperaments on decision-making process of performing an invasive test for Down syndrome. Strengths of the study were the prospective data collection, large number of cases, and diversity of indications for invasive testing. Excluding the babies with major anomalies provided a more homogenous group of patients. With this we had some limitations like not having a healthy control group for comparing the temperament scores, but we tried to overcome this limitation by comparing our results with similar studies with healthy pregnancies. Only  $\leq 5$  years education seemed to be independently associated with not undergoing invasive testing but still our sample size was not large enough to evaluate if other patient and temperament characteristics independently impacted the decision for invasive sampling. Furthermore since our study was not a randomized controlled trial further randomized studies will be helpfull for more accurate information.

In conclusion, our study revealed that a patient's affective temperament profile, in addition to educational and employment status, might play an important role on decision-making processes of accepting or declining an invasive test in case of having an increased risk of Down syndrome fetus. Patients with higher anxious and depressive temperament scores, more likely refused the invasive test, and therefore during prenatal consultation, these psychological profile should be considered in order to provide professional support where needed.

**Yazar Katkıları:** Çalışma konsepti/Tasarımı: EA, GNK, ÇA, DSG, MS; Veri toplama: EA, ÇA; Veri analizi ve yorumlama: EA, GNK, ÇA, DSG, MS; Yazı taslağı: EA, GNK, ÇA, DSG, MS; İçeriğin eleştirilip incelenmesi: EA, DSG; Son onay ve sorumluluk: EA, GNK, ÇA, DSG, MS; Teknik ve malzeme desteği: -; Süpervizyon: EA, DSG; Fon sağlama (mevcut ise): yok.

**Etik Onay:** Bu çalışma için Çukurova Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulundan 13.04.2018 tarih ve 76/75 sayılı kararı ile etik onay alınmıştır.

**Hakem Değerlendirmesi:** Dış bağımsız.

**Çıkar Çatışması:** Yazarlar çıkar çatışması beyan etmemişlerdir.

**Finansal Destek:** Yazarlar finansal destek beyan etmemişlerdir.

**Author Contributions:** Concept/Design : EA, GNK, ÇA, DSG, MS; Data acquisition: EA, ÇA; Data analysis and interpretation: EA, GNK, ÇA, DSG, MS; Drafting manuscript: EA, GNK, ÇA, DSG, MS; Critical revision of manuscript: EA, DSG; Final approval and accountability: EA, GNK, ÇA, DSG, MS; Technical or material support: -; Supervision: EA, DSG; Securing funding (if available): n/a.

**Ethical Approval:** Ethical approval was obtained for this study from the Çukurova University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee with the decision dated 13.04.2018 and numbered 76/75.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** Authors declared no conflict of interest.

**Financial Disclosure:** Authors declared no financial support

## REFERENCES

1. Mai CT, Isenburg JL, Canfield MA, Meyer RE, Correa A, Alverson CJ et al. National population-based estimates for major birth defects, 2010-2014. *Birth Defects Res.* 2019;111:1420-35.
2. Öcal DF TE, Cekmez Y, Gultekin IB, Akdulum MF, Mutlu MF, Biri A. Knowledge level, attitude and behaviours about down syndrome screening among Turkish pregnant women. *Medeniyet Med J.* 2016;31:98-104.
3. Practice Bulletin No. 162: Prenatal Diagnostic Testing for Genetic Disorders. *Obstet Gynecol.* May 2016;127:e108-e122.
4. Theodora M, Antsaklis A, Antsaklis P, Blanas K, Daskalakis G, Sindos M et al. Fetal loss following second trimester amniocentesis. Who is at greater risk? How to counsel pregnant women? *J Matern Fetal Neonatal Med.* 2016;29:590-5.
5. Ternby E, Axelsson O, Annerén G, Lindgren P, Ingvaldstad C. Why do pregnant women accept or decline prenatal diagnosis for Down syndrome? *J Community Genet.* 2016;7:237-42.
6. Sadlecki P, Grabiec M, Walentowicz P, Walentowicz-Sadlecka M. Why do patients decline amniocentesis? Analysis of factors influencing the decision to refuse invasive prenatal testing. *BMC Pregnancy Childbirth.* 2018;18:174.
7. García E, Timmermans DR, van Leeuwen E. The impact of ethical beliefs on decisions about prenatal screening tests: searching for justification. *Soc Sci Med.* 2008;66:753-64.
8. Bromley B, Shipp TD, Lyons J, Groszmann Y, Navathe RS, Benacerraf BR. What is the importance of second-trimester "soft markers" for trisomy 21 after an 11- to 14-week aneuploidy screening scan? *J Ultrasound Med.* 2014;33:1747-52.

9. Nyberg DA, Souter VL, El-Bastawissi A, Young S, Luthardt F, Luthy DA. Isolated sonographic markers for detection of fetal Down syndrome in the second trimester of pregnancy. *J Ultrasound Med.* 2001;20:1053-63.
10. Viora E, Errante G, Bastonero S, Sciarrone A, Campogrande M. Minor sonographic signs of trisomy 21 at 15-20 weeks' gestation in fetuses born without malformations: a prospective study. *Prenat Diagn.* 2001;21:1163-6.
11. Vahip S, Kesebir S, Alkan M, Yazici O, Akiskal KK, Akiskal HS. Affective temperaments in clinically-well subjects in Turkey: initial psychometric data on the TEMPS-A. *J Affect Disord.* 2005;85:113-25.
12. Akiskal KK, Akiskal HS. The theoretical underpinnings of affective temperaments: implications for evolutionary foundations of bipolar disorder and human nature. *J Affect Disord.* 2005;85:231-9.
13. Lutgendorf MA, Stoll KA. Why 99% may not be as good as you think it is: limitations of screening for rare diseases. *J Matern Fetal Neonatal Med.* 2016;29:1187-9.
14. World Medical A. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *Bull World Health Organ.* 2001;79:373-4.
15. Buckwalter JG, Stanczyk FZ, McCleary CA, Bluestein BW, Buckwalter DK, Rankin KP et al. Pregnancy, the postpartum, and steroid hormones: effects on cognition and mood. *Psychoneuroendocrinology.* 1999;24:69-84.
16. Yazici E, Uslu Yuvaci H, Yazici AB, Cevrioglu AS, Erol A. Affective temperaments during pregnancy and postpartum period: a click to hyperthymic temperament. *Gynecol Endocrinol.* 2018;34:265-9.
17. Yazici E, Terzi H, Bosgelmez S, Yazici AB, Zincir SB, Kale A. Affective temperaments in pregnancy. *Gynecol Endocrinol.* 2014;30:894-8.
18. Seror V, L'Haridon O, Bussi eres L, Malan V, Fries N, Vekemans M et al. Women's attitudes toward invasive and noninvasive testing when facing a high risk of fetal down syndrome. *JAMA Netw Open.* 2019;2:e191062.
19. Salomon LJ, Sotiriadis A, Wulff CB, Odibo A, Akolekar R. Risk of miscarriage following amniocentesis or chorionic villus sampling: systematic review of literature and updated meta-analysis. *Ultrasound Obstet Gynecol.* 2019;54:442-51.
20. Weichert A, Braun T, Deutinger C, Henrich W, Kalache KD, Neymeyer J. Prenatal decision-making in the second and third trimester in trisomy 21-affected pregnancies. *J Perinat Med.* 2017;45:205-11.
21. Adiyaman D, Atakul BK, Kuyucu M, Sahingoz Yildirim AG, Pala HG. Termination of pregnancy following a Down Syndrome diagnosis: decision-making process and influential factors in a Muslim but secular country, Turkey. *J Perinat Med.* 2021;49:170-7.
22. Cederholm M, Sj od en PO, Axelsson O. Psychological distress before and after prenatal invasive karyotyping. *Acta Obstet Gynecol Scand.* 2001;80:539-45.
23. Klein DN, Kotov R, Bufferd SJ. Personality and depression: explanatory models and review of the evidence. *Annu Rev Clin Psychol.* 2011;7:269-95.
24. Leykin Y, Roberts CS, Derubeis RJ. Decision-making and depressive symptomatology. *Cognit Ther Res.* 2011;35:333-41.