

# Comparison of Anxiety Levels in Spontaneous Pregnancies and Assisted-Reproductive Techniques

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## ABSTRACT

**Purpose:** Anxiety observed in the perinatal period can have adverse outcomes for the health of the mother and baby. The use of assisted reproductive techniques (ART) has been increasing in recent years for various reasons. In our study, we aimed to compare the anxiety levels of women, who had conceived spontaneously with women who had conceived by ART in these two groups.

**Methods:** 60 pregnant women in their pregnancy, who had applied to the pregnancy and in vitro fertilization (IVF) outpatient clinics, were divided into two groups as follows: those who became pregnant by ART and those who became pregnant spontaneously. The study employed the Beck Anxiety Inventory (BAI), the State and Trait Anxiety Inventory (STAI), and the Perinatal Anxiety Screening Scale (PASS) to assess and identify symptoms of anxiety.

**Results:** Among 60 pregnant women in the study, twenty-four (40%) conceived by ART, and 36 (60%) conceived spontaneously. When the groups were compared with regard to anxiety symptoms, the state anxiety levels of those who became pregnant via ART were significantly higher according to the STAI-S and PASS.

**Conclusion:** As a result, each population should present its own results, and in the event of increased anxiety, appropriate medical assistance should be provided.

**Keywords:** anxiety; assisted reproductive techniques; pregnancy; psychiatry

## ÖZET

**Amaç:** Perinatal dönemde görülen anksiyete anne ve bebek sağlığı açısından olumsuz sonuçlar doğurabilmektedir. Yardımcı üreme tekniklerinin (ART) kullanımı son yıllarda çeşitli nedenlerden dolayı artmaktadır. Çalışmamızda bu iki grupta kendiliğinden gebe kalan kadınlar ile YÜT ile gebe kalan kadınların kaygı düzeylerini karşılaştırmayı amaçladık.

**Yöntemler:** Gebelik ve tüp bebek (IVF) polikliniğine başvuran, gebeliğindeki 60 gebe, YÜT ile gebe kalanlar ve kendiliğinden gebe kalanlar olmak üzere iki gruba ayrıldı. Çalışmada anksiyete semptomlarını değerlendirmek ve tanımlamak için Beck Anksiyete Envanteri (BAI), Durumluk ve Sürekli Kaygı Envanteri (STAI) ve Perinatal Anksiyete Tarama Ölçeği (PASS) kullanıldı.

**Bulgular:** Çalışmaya katılan 60 gebeden 24'ü (%40) YÜT ile, 36'sı (%60) spontan olarak gebe kaldı. Gruplar anksiyete belirtileri açısından karşılaştırıldığında, YÜT ile gebe kalanların durumluk kaygı düzeyleri STAI-S ve PASS'a göre anlamlı derecede yüksekti.

**Sonuç:** Sonuç olarak her popülasyon kendi sonuçlarını sunmalı ve kaygının artması durumunda uygun tıbbi yardım sağlanmalıdır.

**Anahtar Kelimeler:** anksiyete; yardımcı üreme teknikleri; gebelik; psikiyatri

In many societies today, particularly in industrialized societies, infertility has become an undeniable reality as a result of the postponement of marriage and fertility, changing eating habits, smoking, and alcohol consumption (1). With technological developments, the clinical use of assisted reproductive techniques (ART), particularly in-vitro fertilization (IVF), is increasing (2). Despite technological developments, the success of ART is still limited. In the UK, on average one quarter of couples undergoing ART cycles are successful (3). Cost, hormonal injections, physiological changes and medical interventions may cause stress in couples, especially women. If pregnancy occurs, increased prenatal risks may also cause anxiety (4).

Physiological, hormonal, and psychological changes during pregnancy, as well as environmental factors, and pregnancy complications, may cause anxiety in couples (5-7). The prevalence, and effects of anxiety symptoms in the perinatal period are increasingly emphasized (7). As supported by the literature, anxiety observed in the prenatal period has adverse effects on the mother and the baby. It has been reported that anxiety in the perinatal period can cause perinatal and postnatal problems such as low birth weight, preterm birth, and mental health problems in the child (8).

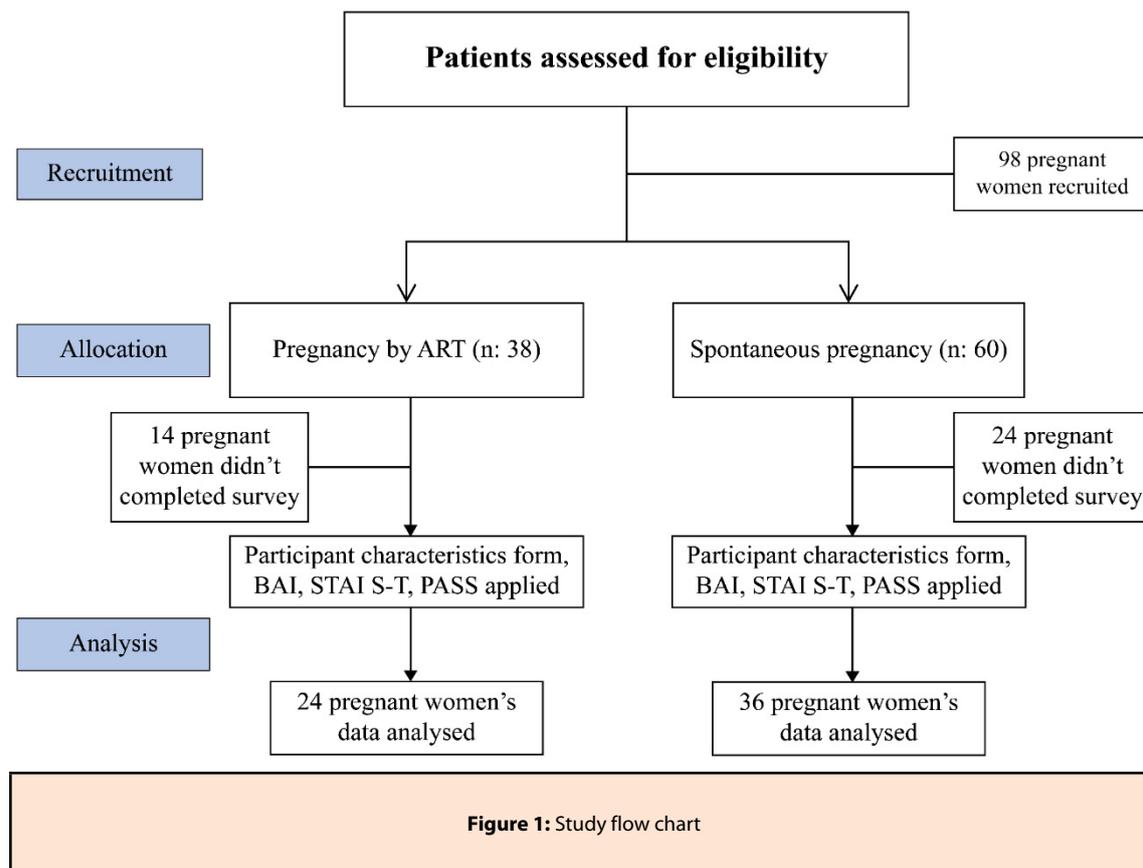
In the literature, contradictory findings were obtained regarding anxiety levels between women, who became pregnant via ART and those who became pregnant spontaneously. Although studies report that anxiety levels are higher in women, who become pregnant via ART than in women who conceive spontaneously (9, 10), there are also studies in which no difference was observed between the two groups (11). Emphasis is placed on the significance of identifying and addressing anxiety during the antenatal period, highlighting a clear need for research in this domain. In this study, we used various anxiety level assessment tests to compare the anxiety levels of pregnant women, who had received ART via IVF with those of pregnant women who had conceived naturally.

## Material and Methods

The study included pregnant women, who applied to Acibadem Atakent Hospital Pregnancy and IVF outpatient clinics. Recruitment took place between March 20, 2023, and May 10, 2023. Pregnant women, who applied to the pregnancy outpatient clinic for antenatal care, met the inclusion criteria, and were between the 12th and 18th gestational weeks, were invited to participate in the study. Women with simultaneous spontaneous pregnancies and IVF pregnancies were invited to participate in the study. In total, 98 women's data (38 IVF, and 60 spontaneous) were obtained, but 14 IVF and 26 spontaneous pregnancies were excluded from the analysis due to incomplete data collection forms. Data from 24 IVF-pregnant women and 36 spontaneous-pregnant women were analyzed, for a total of 60 pregnant women.

All the pregnant women completed the questionnaire independently. An information form containing socio-demographic, clinical, and pregnancy-related features, which was prepared by the researchers in line with the purpose of the study, was filled in. Then, the Beck Anxiety Inventory (BAI), the State and Trait Anxiety Inventory (including State and Trait subscales) (STAI, STAI-S, STAI-T), and the Perinatal Anxiety Screening Scale (PASS) were used (Figure 1).

The study's inclusion criteria were set to include pregnant individuals seeking assistance from Acibadem Atakent Hospital IVF and Pregnancy outpatient clinics, having a singleton pregnancy, being fluent in Turkish, and having no fetal anomalies in the current pregnancy. Exclusion criteria involved illiteracy, severe psychiatric conditions like acute psychotic episodes, mental retardation, and dementia, hindering the ability to provide informed consent. The study received ethical approval from the Acibadem University Ethics Committee under application number 2019-9/9. Verbal informed consent was obtained from all subjects involved in the study. The study data collection was carried out approximately six months after ethics committee's approval.



### Data Collection Forms

#### Participant characteristics form

The questionnaire used to determine the pregnant women's basic demographics was designed by the team before conducting the study. The form encompassed age, education level, infertility period, family income, and partner support.

#### The Beck Anxiety Inventory (BAI)

It is a Likert-type self-assessment scale consisting of 21 items in total and scored between 0-3. A high total score on the scale, designed to assess the severity of anxiety symptoms, indicates an elevated level of experienced anxiety. The validity and reliability study of the scale in Türkiye was performed by Ulusoy et al. (12). The State and Trait Anxiety Inventory (STAI)

A Likert-type scale consisting of 40 questions and two subscales, each containing 20 questions. While State Anxiety (STAI-S) expresses an individual's anxiety related

to a specific stressful situation, Trait Anxiety (STAI-T) indicates the individual's general anxiety level. High scores obtained from the scale indicate a high level of anxiety. The Turkish validity and reliability study of the scale was performed by Öner and Le Compte (13). The Cronbach's alpha value of the scale, validated by Öner and Le Compte, was .83 (13). In our study, the Cronbach's alpha value of the STAI-I was .072.

#### The Perinatal Anxiety Screening Scale (PASS)

The Likert-type scale developed to screen for anxiety symptoms in the perinatal period consists of 31 items. The Turkish validity and reliability study was performed by Yazıcı et al. (14). In our study, the Cronbach's Alpha coefficient of the scale was found to be 0.92.

### Statistical Analysis

The SPSS 26.0 (IBM Corporation, Armonk, New York, United States) program was used to analyze the variables. Cronbach's Alpha coefficient was calculated for the consistency of the scales. The conformity of the data to the

normal distribution was evaluated using the Kolmogorov-Smirnov test. The Mann-Whitney U test was used together with the Monte Carlo results to compare two independent groups according to the quantitative variables. The Fisher Exact test was tested with the Monte Carlo Simulation technique in the comparison of groups according to the categorical variables. Spearman's Rho test was used to examine the correlations of the variables with each other. The Enter method was used in conjunction with the logistic regression test to determine the cause-effect relationship of the groups with the explanatory variables. Quantitative variables were expressed as mean (standard deviation) and median (IQR) (Inter-quartile Range) in the tables, while categorical variables were shown as n (%). The variables were analyzed at a 95% confidence level and a p-value of less than 0.05 was considered significant.

## Results

The mean age of 60 pregnant women included in the study was  $32.1 \pm 4.3$ . Twenty-four (40%) conceived by ART, and the rest (n: 36, 60.0%) were spontaneous pregnancies (planned n: 25, 41.7%; unplanned n: 11, 18.3%). The

majority of the patients had a university/masters-level education (n: 52, 86.7%) and had a moderate income (n: 49, 81.7%). Almost all (n: 58, 96.7%) were nuclear families. Ten women (16.7%) reported a chronic medical illness requiring treatment, while only one (1.7%, Generalized Anxiety Disorder (GAD)) reported receiving treatment for a psychiatric disorder. Although 7 (11.6%) participants did not disclose a diagnosis, FMF was the most common medical disease among patients, who disclosed their diagnosis (n: 2, 3.4%). Of the patients, 9 of them (15%) stated that they had previously received psychiatric treatment. Seven (11.6%) of them reported that they had received treatment for GAD. Most of the sample rated the support they had received from their spouses and peers as "good" (n: 51, 87.9% and n: 46, 79.3%, respectively). Participants, who conceived by ART, were pregnant at a median of 15 weeks (IQR: 13.3), and those, via spontaneous pregnancy, were at a median of 16.5 weeks (IQR: 21.0). There was no significant difference between the groups in terms of gestational times (Mann-Whitney U Test, Z: -0.18, p:0.86). The sociodemographic characteristics of the participants separated by pregnancy method are given in Table 1.

**Table 1:** Sociodemographic characteristics and anxiety symptoms according to the scales applied in women, who conceived spontaneously or by ART.

	Spontaneous	IVF	Impact value	P
	(n: 36)	(n: 24)		
	n (%)	n (%)		
<b>Education</b>			0.32 <sup>a</sup>	<b>0.017</b> <sup>f</sup>
High school	8 (22.2%)	0 (0.0%)		
Bachelor's-Master's Degree	28 (77.8%)	24 (100.0%)		
<b>Income level</b>			-	0.173 <sup>f</sup>
Median	27 (75.0%)	22 (91.7%)		
High value	9 (25.0%)	2 (8.3%)		
<b>Family structure</b>			-	0.512 <sup>f</sup>
Core	34 (94.4%)	24 (100.0%)		
Large	2 (5.6%)	0 (0.0%)		
<b>Medical diseases</b>	3 (8.3%)	7 (29.2%)	-	0.073 <sup>f</sup>
<b>Psychiatric disorders</b>	1 (2.8%)	0 (0.0%)	-	0.999 <sup>f</sup>
<b>Past psychiatric treatment</b>	3 (8.3%)	6 (25.0%)	-	0.137 <sup>f</sup>
<b>Mate support</b>			-	0.999 <sup>f</sup>
Median	4 (11.1%)	3 (13.6%)		
High value	32 (88.9%)	19 (86.4%)		
<b>Social environmental support</b>			-	0.182 <sup>f</sup>
Median	10 (27.8%)	2 (9.1%)		
High value	26 (72.2%)	20 (90.9%)		
	<b>Median (IQR)</b>	<b>Median (IQR)</b>		
<b>STAI-S</b>	39.0 (5.3)	50.0 (13.0)	1.4 <sup>d</sup>	<b>&lt;0.001</b> <sup>u</sup>
<b>STAI-T</b>	45.0 (9.0)	49.0 (6.0)	-	0.490 <sup>u</sup>
<b>PASS</b>	31.5 (8.0)	21.0 (19.0)	0.7 <sup>d</sup>	<b>0.010</b> <sup>u</sup>
<b>BAI</b>	9.0 (14.0)	17.0 (27.0)	-	0.210 <sup>u</sup>

<sup>f</sup> Fisher Exact Test (Monte Carlo), <sup>u</sup> Mann Whitney U Test, <sup>d</sup> Cohen's d, <sup>a</sup> Phi, IQR: Inter-quartile Range

ART: assisted reproductive techniques; IVF: In vitro fertilization; STAI: State and Trait Anxiety Inventory; S: State; T: Trait; PASS: Perinatal Anxiety Screening Scale; BAI: Beck Anxiety Inventory

None of the women, who became pregnant with ART, were high school graduates and did not live with a large family. Only one (1.66%) of the mothers with spontaneous pregnancy reported a psychiatric disorder requiring treatment during evaluation. The groups' education, income level, family structure, social support, and medical/psychiatric diseases were similar. Most of the participants from the sample had their second (n: 32, 53.3%) or first (n: 26, 43.3%) pregnancies. The median number of pregnancies was found to be 2.0 (IQR: 1.0). Most of the participants (n: 42, 70%) had no children. Seventeen participants (28.3%) had one child, while one participant (1.7%) had two children. All patients, who had successful previous pregnancies, had had children via spontaneous pregnancies. Among the participants with spontaneous pregnancies (n: 36), preterm birth in previous pregnancies was reported in 8 (13.1%), abortion in 15 (24.6%), threatened abortion in 2 (3.3%), and induced abortion due to medical complication in 1 (1.6%). The deliveries were spontaneous in 1 (1.6%) of the participants and by caesarean section in 22 (36.1%) participants. In five (8.2%) cases, the baby had a history of inpatient treatment in the Paediatric Intensive Care Unit.

Sixteen participants (26.6%) stated that they breastfed their children for a median of 12 months after previous pregnancies (IQR: 0.0). Two of them (3.3%) reported that they had problems during breastfeeding. Ten (41.7%) of the patients, who had pregnancies via ART reported that they had previously unsuccessful pregnancies. Eight (33.3%) of these resulted in abortion, and two (8.3%) resulted in premature birth and infant loss. There was no significant difference between the groups regarding previous unsuccessful pregnancies (Chi-square (3): 4.9, p: 0.18, Likelihood Ratio). When the participants were evaluated with STAI-S, STAI-T, PASS, and BAI, it was found that the scores of these scales were not generally distributed between the groups (p:0.003, 0.006, 0.001, and 0.01; all Kolmogorov-Smirnov test). Cronbach's alpha was 0.92, 0.88, 0.90, and 0.95 for all sampled scales. Therefore, non-parametric tests were used for comparisons. Scale scores according to pregnancy types are given in Table 1.

As they observed the participants' perspectives, the state anxiety levels of those who became pregnant via ART were found to be high. Pregnancy-related anxieties were found to have a high productivity level in those who conceived spontaneously. For the entire sample, STAI-S scores correlated significantly with PASS (Rho: -0.57, p: 0.00) and BAI (Rho: 0.42, p: 0.04) scores. Controlling gestational age eliminated the association with BAI, but decreased the

association with PASS (Rho: -0.51, n: 0.01; all Spearman's Rho). For participants, who conceived spontaneously, STAI-S correlated significantly with PASS (Rho: -0.42, p: 0.01). However, the significance was not preserved by controlling the gestational age. When the correlations in the participant group, who became pregnant via ART were evaluated, STAI-S scores were found to be associated only with STAI-T scores (Rho: 0.50, p: 0.03). Controlling the gestational age eliminated this association and revealed a significant correlation with PASS scores (Rho: -0.68, p: 0.05).

When the cut-off point for clinically significant anxiety on the PASS was accepted as 16 points [14], 53 (88.3%) participants scored above this cut-off point, finally, logistic regression was applied to evaluate predictors of clinically significant PASS scores. As predictors, STAI-S, gestational age (weeks), pregnancy type (spontaneous vs. ART), complications in previous pregnancies, medical illnesses, and past psychiatric treatment were considered. Each predictor was entered in a separate step, and in the last step, all predictors were analyzed with the Enter method. Although the model was adequate ( $\chi^2$ : 2.1, dF: 7, p: 0.95, Nagelkerke R<sup>2</sup>: 0.41), none of the predictors, alone or in combination, was significant for a clinically significant PASS score (Table 2).

**Table 2:** Predictors of a PASS score above the cut-off point among ART and spontaneous pregnancy samples according to logistic regression analysis.

Predictor	Odds Ratio	95 % CI	p
Previous complications in pregnancy	0	0-	0.999
ART vs spontaneous pregnancy	35.80	0.3-4297.7	0.140
Medical disorder	0.10	0-	0.999
Past psychiatric disorder	0.00	0-	0.999
STAI-S	1.60	0.8- 3.2	0.210
Pregnancy period (week)	1.20	0.8- 1.6	0.420

*Logistic Regression (Enter)*

*STAI-S: The State-Trait Inventory- Self; ART: assisted reproductive techniques; PASS: Perinatal Anxiety Screening Scale*

## Discussion

Every woman should spend the pregnancy period peacefully and comfortably. For a pregnant woman, this journey is filled with uncertainties, and as the pregnancy advances, curiosity may heighten, leading to increased anxiety (15). In the literature, there are many anxiety studies that utilize different scales related to pregnancy and the postpartum period (16, 17). In our study, we aimed to investigate the differences in anxiety levels during pregnancy between women, who spontaneously conceived and women, who conceived with ART and the variables that may be effective.

The importance of screening anxiety symptoms during pregnancy at least once with a standardized method with accepted validity has been emphasized (18). In studies on anxiety during pregnancy, scales commonly used in the general population were used (BAI, STAI) (12, 13). Recently, Somerville et al. developed the PASS, an anxiety screening scale specialized for this period, based on the importance of anxiety in the perinatal period (19). It has been reported that the PASS can detect anxiety in pregnant women at a rate that overlaps with clinical interviews (20). In our study, these three scales were used together to evaluate the level of anxiety in pregnant women.

Gourounti et al. reviewed studies between 2000 and 2014 examining the anxiety levels of women, who conceived spontaneously and of women, who conceived via ART (21). As a result, she discovered that women, who became pregnant following ART experienced increased pregnancy-specific anxiety, a lower quality of life, the same or fewer depressive symptoms, and the same level of self-confidence. In addition, it was found that prenatal attachment levels were higher. Oftedal et al. conducted a cohort study in Norway comparing 2,960 ART pregnancies with 108,183 spontaneous pregnancies (22). Accordingly, both females and males had lower levels of anxiety and depression in ART pregnancies compared to those in spontaneous pregnancies.

Since the PASS scale includes worries and fears about the baby and pregnancy and general questions about anxiety, it suggests the existence of primary concerns about the baby's health and the pregnancy process. As pregnancy progresses, anxiety may increase due to uncertainty, and studies show that anxiety decreases as the gestation period progresses (18). In our study, sociodemographic

and pregnancy-related variables that may predict perinatal anxiety were analyzed, and it was found that variables such as gestation period (weeks), complications in previous pregnancies, and medical diseases alone were insufficient to predict perinatal anxiety. When these variables were considered together, it was thought that they could be used as a model for determining perinatal anxiety. In our study, when the cut-off point for perinatal anxiety assessed by PASS was accepted as 16 points (14), it was found that most participants (88.3%) had high anxiety levels. This rate is generally higher than the literature, suggesting that the PASS is a sensitive tool in determining perinatal anxiety (23, 24). As stated in our study, perinatal anxiety levels determined by PASS were high in both groups. However, the pregnancy-related anxiety of the spontaneously pregnant participants was significantly higher than the other group. Since the PASS scale includes worries and fears about the baby and pregnancy and general questions about anxiety, it suggests the presence of primary concerns about the baby's health and the pregnancy process in this group. The literature has reported that some sociodemographic and pregnancy-related variables may be related to anxiety.

The study of Stevenson et al. was conducted with a smaller number of patients (25). STAI and PRAM questionnaires were administered to men and women in all trimesters. The study's results revealed that the anxiety levels of couples, who conceived through IVF and couples, who conceived naturally were comparable. Stress levels were also found to increase in men as the trimester progressed while decreasing in women. In our study, anxiety in men was not examined and a questionnaire was applied only once for pregnant women. Darwiche et al. also compared IVF/ICSI pregnancies with spontaneous pregnancies before first-trimester screening on a more limited number of pregnant women (26). A study using STAI and several different samples discovered that the group, who became pregnant with ART, had higher STAI scores. Our study found that the state anxiety scores determined by STAI-S were significantly higher in women, who conceived via ART (mean 50 points vs 39 points). The state anxiety score of those who conceived via ART was also significantly higher than those who conceived spontaneously.

In the literature, a history of psychiatric illness has been reported as a risk factor for anxiety (18), and in our study, only one pregnant woman had a history of psychiatric illness. Furthermore, the sociodemographic, clinical, and

pregnancy-related characteristics of the patients in our study allowed for the formation of comparable groups, facilitating a meaningful comparison between the two groups. The fact that most of the patients had bachelor's/master's degrees increased the likelihood of an adequate response. Although studies in the literature show that prenatal screening tests performed to evaluate fetal health increase anxiety (27, 28), the relationship of this variable with anxiety was not investigated in our study. If anxiety symptoms are detected in pregnant women, seeking help from psychiatry for detailed evaluation and follow-up is essential.

## Limitations

The study's cross-sectional design, the fact that it was conducted in a single center, being exclusively for women and applied only once, and the small number of cases do not allow for generalization of the results.

## Conclusions

When the literature is examined, anxiety assessments of women, who conceived via ART and women, who conceived spontaneously show different results with different tests. Accordingly, each population should evaluate its own results. If anxiety symptoms are detected in pregnant women, it would be appropriate to seek help from the psychiatry department.

## Declarations

### Funding

There is no funding.

### Conflict of Interest

There is conflict of interest.

### Ethic Approval

The study received ethical approval from the Acibadem University Ethics Committee under application number 2019-9/9.

### Availability of data and material

All data available.

## Author Contributions

Aygün EG: Original draft, formal analysis, writing. Agirbas Ozer U: Study design and protocol, data curation, writing. Sancak B: Study design and protocol, data curation

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