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Evaluation of the Opinions and Anxiety Levels of Female Breast Cancer Patients Receiving Outpatient Chemotherapy Regarding Fertility

Ayaktan Kemoterapi Alan Meme Kanserli Kadın Hastaların Doğurganlığa İlişkin Görüş ve Kaygı/Depresyon Düzeylerinin Değerlendirilmesi

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Abstract

Objectives: As screening and treatment for breast cancer advance, an increasing number of young patients are confronting treatment-related infertility. The aim of this study was to analyze patients' opinions on fertility, and to assess the impact of these opinions on their depression and anxiety levels.

Materials and Methods: The study was designed as a prospective, single-center cohort survey. A total of 63 female patients with breast cancer who were receiving treatment at the Outpatient Units of Medical Oncology at Ankara University were enrolled. The questionnaire included components such as patients' perspectives on fertility, demographic data, and the Hospital Anxiety and Depression Scale (HADS).

Results: The median age was 39 (minimum-maximum: 28-45). Among the patients with metastatic and early-stage breast cancer, anxiety and depression scores were similar (p=0.09). Individuals who believed that having a child posed a risk to their disease had higher HADS scores (p=0.009). Factors identified as increasing the risk of anxiety and depression included being young (<40 years old), being married, unemployment, having a child, and the fear of disease recurrence. After diagnosis, the desire to have children diminished due to concerns about disease recurrence or progression. It was found that 51% of the patients considered the information provided on fertility to be sufficient.

Conclusion: It was observed that providing information on fertility during the treatment process was sufficient for half of the patients. A significant proportion of these patients had children prior to their diagnosis. The majority of patients did not have plans for childbirth, and did not express notable concerns regarding fertility.

Keywords: Breast cancer, fertility, HADS, anxiety, depression

Öz

Amaç: Meme kanseri tarama ve tedavisi ilerledikçe artan sayıda genç hasta, tedaviye bağlı fertilite sorunlarıyla karşı karşıya kalıyor. Bu çalışmanın amacı, hastaların doğurganlık konusundaki görüşlerini analiz etmek ve bu görüşlerin depresyon ve anksiyete düzeylerine etkisini değerlendirmektir.

Gereç ve Yöntem: Çalışma prospektif, tek merkezli bir kohort araştırması olarak tasarlandı. Anket, Ankara Üniversitesi Tıbbi Onkoloji Polikliniği'nde tedavi gören 63 meme kanseri kadın hastaya uygulandı. Ankette, hastaların demografik verileri ve doğurganlık hakkında görüşlerinin yanı sıra Hastane Anksiyete ve Depresyon Ölçeği (HADS) de yer aldı.

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Bulgular: Metastatik ve erken evre meme kanserli hastalar arasında anksiyete ve depresyon skorları arasında anlamlı fark gözlenmedi (p=0,09). Çocuk sahibi olmanın hastalıkları açısından risk oluşturduğuna inanan bireylerin ortalama HADS puanı daha yüksekti (p=0,009). Anksiyete ve depresyon riskini artıran faktörler arasında genç olmak (<40 yaşında), evli olmak, işsizlik, çocuk sahibi olmak ve hastalığın tekrarlama korkusu yer aldı. Teşhis konulduktan sonra hastalığın tekrarlaması veya ilerlemesi endişesi nedeniyle çocuk sahibi olma isteğinin azaldığı izlendi. Hastaların %51'i, doğurganlık konusunda tedavi sürecinde verilen bilgilerin yeterli bulduğu belirtti.

Sonuç: Anksiyete ve depresyon riskini artırdığı belirlenen faktörler arasında genç olmak (<40 yaş), evli olmak, işsizlik, çocuk sahibi olmak ve hastalığın tekrarlama korkusu yer alıyor. Tedavi sürecinde doğurganlık konusunda bilgilendirmenin hastaların yarısı için yeterli olduğu görüldü. Aktif kemoterapi alan ve çok genç yaşta olmayan bu hastaların önemli bir kısmının tanı öncesinde çocuk sahibi olduğu, doğum planı olmadığı ve doğurganlığa ilişkin belirgin bir endişe dile getirmedikleri görüldü.

Anahtar Kelimeler: Meme kanseri, fertilite, HADS, anksiyete, depresyon

Introduction

Breast cancer is the most prevalent malignancy observed in women in Türkiye (1). Through breast cancer screening programs, early-stage detection of patients is achievable. Chemotherapy is commonly administered in operable patients diagnosed at early-stage, as well as in those with locally advanced or metastatic disease, and in cases of recurrence (2,3). Notably, 4-6% of these women are diagnosed during their reproductive years (4). Consequently, fertility-preserving strategies are implemented prior to chemotherapy in adolescent and young adult women diagnosed with cancer, particularly breast and gynecological cancers (5). Fertility-preserving approaches vary based on the social and cultural characteristics of patients, the type of cancer, and the specific treatment and chemotherapy regimens (5). The urgency to initiate cancer treatment promptly, in particular, introduces psychosocial challenges that often accompany the diagnosis (6).

Chemotherapeutic agents, a common treatment option for breast cancer, can also have detrimental effects on fertility (7). There is currently no clear data regarding how patients' and their partners' perspectives on fertility evolve during and after chemotherapy, nor on the factors influencing these views. Furthermore, the factors that determine patients' choice of individuals with whom they feel comfortable discussing and sharing fertility-related concerns following a breast cancer diagnosis remain unknown. Breast loss during the treatment process can significantly impact patients' perception of their female identity (8). When all contributing factors are considered, challenges related to sexual life in women with breast cancer may lead to marital discord and, in some cases, even divorce.

In recent years, fertility has increasingly been emphasized and, at times, used as a means of societal pressure on women (9). Such emphasis can exacerbate psychosocial challenges for women with breast cancer during their reproductive years, potentially intensifying the emotional burden of their diagnosis and treatment (10).

In our country, no research has been conducted that explores the views of women with breast cancer regarding fertility. Furthermore, only two studies in the existing literature has examined patients' perspectives on fertility and anxiety (11,12). The aim of this study was to assess the opinions and knowledge related to childbearing, as well as the depression and anxiety levels, of young female breast cancer patients who had undergone chemotherapy.

Materials and Methods

Study Design and Participants

The study was designed as a prospective, single-center cohort survey. This observational real-life study included a total of 63 breast cancer patients treated between March 1, 2017, and March 30, 2018, at the outpatient unit of Medical Oncology at Ankara University. The study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki, revised in 2013, and was approved by the Ankara University Clinical Research Ethics Committee (decision no.: 12-742-17, date: 24.07.2017). Inclusion criteria were: being a woman aged 18-45, diagnosed with breast cancer, and undergoing chemotherapy and/or hormone therapy. The exclusion criterion was the presence of a neuropsychiatric condition that precluded the completion of the survey form.

Data Collection and Laboratory Measurements

The demographic characteristics of the patients, who provided written informed consent in the consultation room with a clinical psychologist at the medical oncology clinic, were assessed along with factors influencing their fertility and anxiety before, during, and after cancer treatment. These factors were evaluated through survey questions conducted via face-to-face interviews. Data related to the diagnosis, date of diagnosis, treatment modalities applied (surgery, chemotherapy, radiotherapy, hormonal therapy), active disease status, and remission status were collected from the patient database. Anxiety and depression levels were measured using the Hospital Anxiety and Depression Scale (HADS).

Assessments of Anxiety and Depression

HADS is an assessment tool developed by Zigmond and Snaith (13) to identify the risk of anxiety and depression, as well as to measure changes in their severity. The scale was specifically designed to screen for mood disorders in populations with medical conditions. It is widely used in both community and hospital settings due to its simplicity. HADS is a Likert-type scale consisting of 14 questions, with odd-numbered items assessing anxiety and even-numbered items assessing depression.

The validity and reliability of the Turkish version of the HADS were established by Aydemir et al. (14), demonstrating that the scale is effective for screening depression and anxiety symptoms in patients with physical illnesses. The scale includes two subscales: anxiety (HAD-A) and depression (HAD-D). Based on the study conducted in Türkiye, the cut-off score for the anxiety subscale was determined to be 10/11, and for the depression subscale, 7/8. Scores above these thresholds indicate individuals at risk. The scoring of each item on the scale varies accordingly. Items 1, 3, 5, 6, 8, 10, 11, and 13 on the scale indicate progressively decreasing severity, with scores assigned as 3, 2, 1, and 0. Conversely, items 2, 4, 6, 8, 10, 12, and 14 are scored in ascending order as 0, 1, 2, and 3. The total scores for each subscale are calculated by summing the scores of the relevant items. For the anxiety subscale, scores from items 1, 3, 5, 7, 9, 11, and 13 are aggregated, whereas for the depression subscale, scores from items 2, 4, 6, 8, 10, 12, and 14 are combined. The depression subscale consists of seven items, with scores ranging from 0 to 21. The possible scores on both subscales range from 0 to 21, with cut-off points for mood disorder severity classified as follows: 0-7 indicates normal, 8-10 indicates mild, 11-14 indicates moderate, and 15-21 indicates severe mood disorder (3-5).

Statistical Analysis

The appropriate sample size for the study was calculated to be 74, with 80% power and a 5% type-1 error rate. Data analysis was performed using SPSS version 17.0 software. Descriptive statistics were presented as frequencies (n) and percentages (%). Numerical variables that exhibited a normal distribution were reported as mean ± standard deviation, while those that did not follow a normal distribution were reported as median (minimum-maximum) values. The chi-square or Fisher's exact test was used for categorical variables, and the Mann-Whitney U or Kruskal-Wallis test was employed for continuous variables. The independent samples t-test was used to compare parametric variables between two groups. For comparisons involving more than two groups, the significance of differences in mean values was assessed using the One-Way ANOVA test. A 5% type I error level was adopted to determine statistical significance.

Results

Demographic Characteristics of the Patients

A total of 63 female patients participated in the study. All participants completed the study questionnaire and HADS. Among the patients, 47 (75%) were diagnosed with early-stage breast cancer, while 16 (25%) had advanced-stage breast cancer. Sixteen patients (25%) were single or divorced, and 47 patients (75%) were married. Of the patients, 31 (49%) were university graduates, whereas 32 (51%) did not hold a university degree. Additionally, 25 patients (40%) were employed, and 38 patients (60%) were not working. Forty-five patients (71%) had children, while 18 patients (29%) were childless. The characteristics of the patients are summarized in Table 1.

Patients' Opinions About Fertility

Among the survey questions posed to the patients, 7 (11%) answered "yes" and 56 (89%) answered "no" or were undecided regarding the question, "Do you plan to have children after the diagnosis?" Of the 56 patients, 43 (77%) had undergone surgery, while 13 (23%) had metastatic disease. When asked whether they were concerned that having children might pose a risk, 34 patients (22 operated, 12 metastatic) responded "yes", while 29 patients (46%) responded "no". Additionally, 48 patients (76%) indicated that they were not influenced by external opinions regarding having a sick child, whereas 15 patients reported being influenced by their family members. Among the patients who reported being influenced by their relatives or friends, 49 (78%) stated that their desires regarding having children remained unchanged, while 14 (22%) indicated that their desires had either increased or decreased. There was no statistically significant difference between early-stage and advanced-stage patients regarding their responses to questions about fertility. The patients' responses to questions concerning fertility are summarized in Table 2.

Table 1: Demographics and disease characteristics of the patients (n=63)

Characteristics	n (%)
Age, median (minimum-maximum), years	39 (28-45)
Female, n (%)	63 (100)
Married, n (%)	47 (75)
Education status, n (%)	
Graduated from a university	31 (49)
Working status, n (%)	
Active worker	25 (40)
The stage of breast cancer, n (%)	
Early stage cancer	47 (75)
Advanced stage cancer	16 (25)
Patients with children, n (%)	45 (71)

Table 2: The percentage of patients' who answered the following questions on fertility positively

The patients' views	Metastatic, (n=16) (25%)	Operated, (n=47) (75%)	p-value
Are you worried about being in danger if you planned to have a child after your chemotherapy was completed.	12 (75)	22 (47)	0.81
Have your ideas about having a child changed?	3 (19)	11 (23)	1
Have your idea of having a child in the future changed after being diagnosed with breast cancer?	9 (56)	13 (28)	0.66
Would you like to have a child after breast cancer treatment?	3 (19)	4 (8)	0.35
Are there any influences from people around you about having a child?	10 (63)	38 (81)	0.18

Patients' Opinions About Fertility

The patients were asked whether they had been informed by the treatment team about the recommendation to avoid pregnancy during treatment. Twenty-two patients (35%) answered "no", while forty-one patients (65%) answered "yes". Of those who received information, 20 patients (31%) reported that they were informed solely by a medical oncologist, whereas 43 patients (69%) indicated that they received information from a combination of a surgeon, psychologist, and nurse. When asked about the adequacy of the information provided, 32 patients (51%) responded "yes", while 31 patients (49%) answered "no" or were undecided. Regarding whether they received information from additional sources about avoiding pregnancy and having children, 30 patients (48%) reported that they did not receive any additional information, whereas 33 patients (52%) stated that they obtained information from other sources.

No significant difference was observed between early-stage and advanced-stage patients regarding their responses to questions evaluating their opinions on the information provided about fertility. The patients' answers to these questions are summarized in Table 3.

Patients were asked whether they used any contraceptive methods before and after their diagnosis of breast cancer. Twenty-six patients (41%) reported using contraceptives, while 37 patients (59%) stated that they did not use any contraceptive methods. When inquired about the importance of having children, 25 patients (40%) indicated that it was unimportant, 10 patients (16%) were undecided, 6 patients (9%) considered it slightly important, 9 patients (14%) deemed it important, and 13 patients (21%) regarded it as very important. Additionally, among the metastatic patients, 5 (31%) considered having children unimportant, 3 (19%) were undecided, 2 (12%) considered it slightly important, 3 (19%) deemed it important, and 3 (19%) regarded it as very important. In contrast, among the operated patients, 20 (43%) viewed having children as unimportant, 7 (15%) were undecided, 4 (8%) considered it slightly important, 6 (13%) deemed it important, and 10 (21%) regarded it as very important. When asked about the importance of having children for their spouses, 13 patients (19%) considered it unimportant, 26 patients (41%) were undecided, 3 patients (5%) considered it slightly important, 10 patients (16%) deemed it important, and 12 patients (19%) regarded it as very important. Among those who considered having children very important, 33% were from the metastatic group and 67% were from the operated group.

Table 3: Patients' views on fertility information taken from the hospital

I believe I am well informed about risks that may occur in a possible pregnancy, n (%)	32 (51)
I gathered additional information on becoming preganant from sources other than the hospital, n (%)	33 (52)

Hospital Anxiety and Depression Scale Results

The average HADS score for the metastatic group was 12 (range: 5-24), while the average HADS score for early-stage breast cancer patients was 15 (range: 1-36). No significant difference was observed between the HADS scores of the two groups (p=0.09). Twenty-six percent of the patients were identified as being at risk for anxiety, and 34% were at risk for depression. Married individuals were found to be at a higher risk for both anxiety and depression compared to single or divorced individuals (p=0.006). No significant difference in anxiety and depression was observed between patients with a university degree and those without (p=0.054). Working patients had a lower risk of anxiety and depression compared to unemployed patients (p=0.02). Although patients who wanted to have children after their diagnosis had higher HADS scores, this difference was not statistically significant compared to those who did not wish to have children or were undecided (p=0.63). There was no significant difference in HADS scores between patients who were influenced by their relatives regarding having children and those who were not (p=0.98). Among patients influenced by their relatives, no difference in HADS scores was found between those whose desires changed and those whose desires remained unchanged (p=0.63).

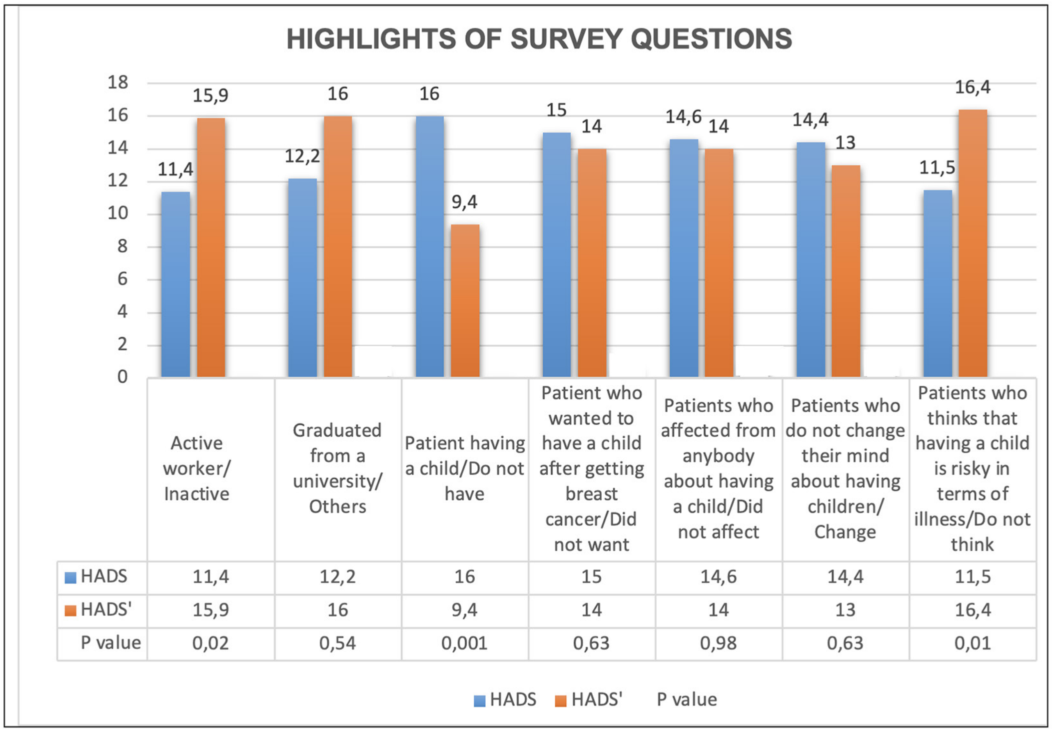
There was no significant difference in HADS scores between patients who were informed about pregnancy and those who were not during their treatment (p=0.76). Patients who believed that having children would pose a risk to their disease had higher HADS scores (p=0.01). No significant difference was observed between the HADS scores of patients who used contraceptive methods before their breast cancer diagnosis and those who did not (p=0.19). Similarly, HADS scores were comparable between those who used contraceptive methods after their breast cancer diagnosis and those who did not (p=0.63). The HADS scores of patients who changed their views about having children after diagnosis were similar to those who did not change their views (p=0.95). The relationship between certain clinical features of the patients and HADS scores is illustrated in Figure 1.

Discussion

The risk of anxiety and depression was found to be comparable between patients diagnosed with early-stage and advanced-stage breast cancer. Among these patients, 26% were identified as being at risk for anxiety, and 34% were at risk for depression. Notably, patients under the age of 40 and those who were married exhibited higher levels of anxiety compared to their single or divorced counterparts. Additionally, individuals who perceived childbearing as a potential risk to their health showed higher HADS scores. Married patients with advanced-stage breast cancer experienced higher levels of anxiety compared to their unmarried counterparts. Similarly, patients with children experienced higher levels of anxiety compared to those without children. Factors associated with an increased risk of anxiety and depression include being under 40 years of age, being married, unemployment, having children, and fearing disease recurrence. A total of 51% of patients reported that they found the information provided about fertility to be sufficient, while 48% indicated that they sought additional resources for information on having children. The risk of anxiety and depression was lower in patients who were employed compared to those who were unemployed.

Studies conducted by Delgado-Guay et al. (15), Saboonchi et al. (16), and Spencer et al. (17) have identified that patients with high anxiety and depression scores are often those with chronic illnesses, particularly individuals with advanced-stage breast cancer (15-17). In the present study, no comparison was made between patients with other chronic illnesses and those diagnosed with cancer, and the sample size in the cited studies exceeded 200 patients. Additionally, Linden et al. (18), in their study involving 2,250 breast cancer patients, demonstrated that anxiety levels were three times higher compared to those in the general population. However, it is important to note that this study did not include a direct comparison with the general population.

Park et al. (19) administered the HADS to 54 women with metastatic breast cancer and found that 28% of the patients were at risk for anxiety, while 20% were at risk for depression.



	Active worker/ Inactive	Graduated from a university/ Others	Patient having a child/Do not have	Patient who wanted to have a child after getting breast cancer/Did not want	Patients who affected from anybody about having a child/Did not affect	Patients who do not change their mind about having children/ Change	Patients who thinks that having a child is risky in terms of illness/Do not think
■ HADS	11,4	12,2	16	15	14,6	14,4	11,5
■ HADS'	15,9	16	9,4	14	14	13	16,4
P value	0,02	0,54	0,001	0,63	0,98	0,63	0,01

Figure 1: Some important HADS scores of the participants

*HADS: Hospital Anxiety and Depression Scale

**HADS': Hospital Anxiety and Depression Scale after informed about pregnancy

HADS: Hospital Anxiety and Depression Scale

Compared to our study, anxiety levels were higher and depression levels were lower in their cohort. Similarly, Akel et al. (20) observed that anxiety was more prevalent than depression among breast cancer patients. Both studies highlighted that factors contributing to higher HADS scores included being of White ethnicity and having a higher level of education (20).

Consistent with the findings of Linden et al. (18), our study also demonstrated that younger patients (under 40 years of age) exhibited higher levels of anxiety and depression. In a single-center study conducted by Kostev et al. (21) in Germany, the anxiety and depression levels of patients diagnosed with breast or genital organ cancer were assessed. The study found that patients, with an average age of 49.3 years, were 1.32 times more likely to experience anxiety and depression compared to individuals without cancer.

Nilsson et al. (22) demonstrated that patients with children had higher levels of anxiety and depression compared to those without children, a finding that is consistent with the results of our study. In our study, patients who perceived having children as a potential risk for disease recurrence had higher HADS scores. Similarly, in a study by Starreveld et al. (23), 267 patients who underwent breast surgery were followed for 18 months to investigate factors influencing fear of recurrence. The study found that educated, married, and optimistic women experienced less fear of recurrence. While individuals with a university education tended to have higher HADS scores compared to those without a university degree, employed patients exhibited significantly lower HADS scores compared to their unemployed counterparts. The reasons for unemployment among patients with high HADS scores were not investigated, as this was not within the scope of our study.

In the study conducted by Peate et al. (24), 120 newly diagnosed breast cancer patients were assessed regarding their future fertility perspectives, decision-making conflicts, decision regret, and treatment satisfaction. Interviews were conducted at 1 month and at 12 months. It was found that those who received assistance during their decision-making process experienced a reduction in regret over the course of the year. Patients expressed satisfaction with receiving information about effective treatments for fertility preservation. In our study, patients were surveyed shortly after diagnosis while undergoing active treatment, and their opinions were collected; however, no follow-up survey was conducted. Nevertheless, 51% of the patients indicated that the information provided regarding fertility was sufficient (as shown in Table 3).

Abe et al. (25) investigated the fertility-related perspectives of 112 breast cancer patients aged 15-40, in collaboration with gynecologic oncologists and oncologists. The study revealed that patients were inadequately informed about fertility due to concerns that fertility preservation might delay cancer treatment. This lack of information was attributed to poor communication between patients and doctors. The study emphasized the importance of oncofertility counseling. In our study, 49% of patients reported not seeking additional information about fertility, while 43% indicated that they had received information from at least one medical oncologist.

Conclusion

As a conclusion, it has been determined that the information on fertility is sufficient. Factors that increase the risk of anxiety and depression in breast cancer patients of reproductive age include being younger (under 40 years old), being married, not being employed, having children, and fear of recurrence. A significant proportion of these patients, who were undergoing active chemotherapy and were not of a very young age, had children prior to their diagnosis. The majority of patients did not have plans for childbirth, and it was observed that they did not express notable concerns regarding fertility.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki, revised in 2013, and was approved by the Ankara University Clinical Research Ethics Committee (decision no.: 12-742-17, date: 24.07.2017).

Informed Consent: Informed consent was obtained from all the participants in the consultation room with a clinical psychologist at the medical oncology clinic.

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Footnotes

Authorship Contributions

Concept: G.T., A.A., F.Ç.Ş., Design: G.T., A.A., F.Ç.Ş., Data Collection and/or Processing: G.T., Analysis and/or Interpretation: G.T., A.A., F.Ç.Ş., Literature Search: G.T., Writing: G.T., A.A., F.Ç.Ş.

Conflict of Interest: According to the authors, there are no conflicts of interest related to this study.

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