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Sexual Function in Postmenopausal Women with Urinary Incontinence and Pelvic Organ Prolapse

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ABSTRACT

Objective: This study aims to investigate the frequency of pelvic organ prolapse and urinary incontinence and their effects on sexual function.
Material and Method: This descriptive and cross-sectional study included 605 women in their climacteric period who were admitted to a hospital in Istanbul, between April 2018 and January 2019. The data was collected by a structured questionnaire form with 37 questions and pelvic organ prolapse/urinary incontinence sexual function questionnaire scale (PISQ-12).
Results: The incidence of urinary incontinence (43.1%) and pelvic organ prolapse (protrusion 24.3%; bulging 16.4%) was noticeably high in postmenopausal women. The mean score of PISQ-12 was 29.43 ± 3.51. The women with urinary incontinence (p=0.008) and pelvic organ prolapse (p=0.000) had lower PISQ-12 scores in comparison to those without urinary incontinence and pelvic organ prolapse.
Conclusion: The incidence of urinary incontinence and pelvic organ prolapse was noticeably high in postmenopausal women. The women with urinary incontinence and pelvic organ prolapse had lower sexual function scores.
Keywords: Postmenopausal, sexual function, urinary incontinence, pelvic organ prolapse

INTRODUCTION

Significant loss of estrogen with menopause results in physical problems such as atrophy, prolapse, and incontinence in genitourinary tissues. These physical symptoms, which are part of the newly termed menopause genitourinary syndrome (menopause-GS), negatively affect women in all aspects of their lives (1,2). The most frequently observed genitourinary problems include pelvic organ prolapse (POP) and urinary incontinence (UI) (3,4).

Problems such as vaginal obstruction, coital incontinence, and dyspareunia that result from POP and UI, adversely affect female sexual function (5). In their study, Gupta et al. (6) reported that one-third of the women with POP showed signs of sexual dysfunction such as loss of libido, anorgasmia, vaginal dryness, and dyspareunia. In a study conducted by Yesiltepe et al. (7), 83.6% of sexually active women with UI had lower libido and frequency of sexual intercourse. According to the study by Grzybowska and Wydra (8), 65% of 289 women with stress urinary incontinence experience coital incontinence. Evaluation of the incidence of POP and UI in the postmenopausal period and its effects on sexual function will help healthcare professionals improve women's physical, social, and mental health and quality of life. This study aims to determine sexual function in postmenopausal women with urinary incontinence and pelvic organ prolapse.

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MATERIAL AND METHODS

Study Design

It was designed to be descriptive and cross-sectional. The study sample included menopausal women admitted to a university hospital's gynecology Clinic in Istanbul between April 2018 and January 2019. The study sample included 605 volunteers meeting the inclusion criteria, which was initially determined as 600 individuals by means of power analysis 3.1.7 at 95% confidence interval, 5% error term, and an effect size of 0.5 with 80% power.

The inclusion criteria were as follows; willingness to participate, being in postmenopausal period, sexually active, and knew Turkish. Women who had neurological problems were excluded from the study.

Data Collection Tools

The study data was obtained through a pelvic organ prolapse/urinary incontinence sexual function questionnaire scale (PISQ-12) questioning the presence of pelvic organ prolapse and urinary incontinence and their effect on sexual function and through another questionnaire of 37 questions prepared by the researcher, which contain menopause-related, obstetric and gynecological information, and investigate the symptoms of urinary continence (enuresis, nocturia, incontinence during activities such as coughing and so forth) and pelvic organ prolapse (bulging and protrusion in the genital organ) in line with the literature (1,9,10).

Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire Scale (PISQ-12): It is a questionnaire form that evaluates sexual function in women with urinary incontinence and/or pelvic organ prolapse and includes 12 questions. The questions that constitute the questionnaire are divided into subgroups: 1 to 4 behavioral-emotional, 5 to 9 physical, and 10-12 partner-relationship. The answers given to the questions in each topic are scored between 0-4. The maximum total score of this questionnaire consisting of 12 questions is 48. Higher scores indicate higher sexual function (11). Turkish validation of the scale was carried out by Cam et al. (11) in 2009 and the internal consistency of Cronbach alpha was found to be 0.89. In this study, the internal consistency coefficient of Cronbach alpha of the PISQ-12 was 0.79.

Study data was collected utilizing a face-to-face interview technique.

Data Analysis

The study data was evaluated using the Statistical Package for the Social Sciences (SPSS) (Windows 15.0) package program. For the statistical analysis of data, descriptive statistical methods (mean, standard deviation, mode, median, frequency, minimum, maximum) and Mann Whitney U and Chi-Square tests were used.

Ethical Approval

Ethical approval was obtained from Zeynep Kamil Gynecology and Pediatric Training and Research Hospital's Clinical Research Ethics Committee (Ethics Committee Number: 23, July 2018). The data was collected after obtaining informed consent from the participants and having them sign the Informed Consent Form.

RESULTS

The mean age of the women who participated in the study was 54.52 ± 9.59. Most of the women (71.9%) were primary school graduates, and 42.3% were found to be obese (> 25) according to body mass index. When the obstetric data of women was examined, it was found that 79.7% of women had had 2 or more pregnancies. Of these, 52.2% had their deliveries in a hospital, 71.4% had a vaginal delivery, 48.9% of women underwent episiotomy during labor and 40.8% of them received oxytocin induction during delivery. Other information about the demographic, obstetric, and gynecological data of the women is given in Table 1.

Of all the women in the study, 66.9% were found to be in a menopausal period for 10 years or below. It was found that only 19% were taking hormone therapy (HT), 34.5% had a daily urine count above 6 and 26.9% had enuresis. When the data on UI was examined, it was found that 43.1% (n=261) of women had an involuntary loss of urine and 96.2% of these women had this complaint for 5 years or less. It was found that 34.3% of women with UI experience incontinence once a day. It was found that 28.8% of women with UI showed the symptoms of stress urinary incontinence, 23.7% had urge urinary incontinence, and 47.5% experienced mixed urinary incontinence. When the findings of POP were examined, it was found that 24.3% (n = 147) of the women had vaginal prolapse, and 16.4% (n = 99) of women had vaginal bulging (Table 2).

The PISQ-12 score was 29.43 ± 3.51, and the lowest score was found to be related to the partner-relationship factors section (4.42 ± 1.58). When the women with and without UI were compared in terms of PISQ-12 scales, a higher PISQ-12 scale score was determined in women without urinary incontinence. (Z_{MWU}: -4.798, p=0.008). When the data was examined in terms of the sub-dimensions, scale scores were higher in those without UI in terms of partner-relationship factors (Z_{MWU}: -3.491, p=0.000), behavioral-emotional factors (Z_{MWU}: -2.659, p=0.008) and physical factors (Z_{MWU}: -2.634, p=0.008) (Table 3). Women who did not have POP symptoms had a higher total PISQ-12 score compared to women without POP symptoms (Z_{MWU}: -4.152, p=0.000). When examined in terms of the sub-dimensions, there was a statistically significant relationship in terms of physical factors (Z_{MWU}: -7.786, p=0.000) and partner-relationship factors (Z_{MWU}: -2.604, p=0.009). However, there was no significant difference in terms of behavioral-emotional factors (Z_{MWU}: -1.898, p=0.058) Accordingly, the physical factor and partner-relationship factor sub-dimension scores were higher in women without POP (Table 3).

Women with a body mass index >25 (obese) (χ^2=6.814, p=0.009) and who had chronic constipation (χ^2=60.582, p=0.000) were found to have more UI symptoms. It was found that UI was seen more frequently in women who had POP symptoms (χ^2=49.029, p=0.000). Additionally, it was found that UI was seen more frequently in women who had had gynecological surgery (χ^2=18.067, p=0.000). In women who had UI, a significant difference was found in terms of the number of deliveries compared to those without UI (χ^2=6.960, p=0.008). Accordingly, multiparous women showed more symptoms of urinary incontinence than primiparous and nulliparous women. When the type of delivery was examined, it was determined that women with UI had more vaginal deliveries (χ^2 = 41.182, p= 0.000). More UI symptoms were observed in women who did not undergo episiotomy (χ^2=8.444, p=0.004) during labor and

Table 1: Demographic, obstetric and gynecological characteristics of women (n=605)

Variables	n	%
Age		
32-45	110	18.2
46-65	412	68.1
66 or above	83	13.7
Level of Education		
Non-literate	11	1.8
Primary School	435	71.9
High School	114	18.8
Undergraduate or above	45	7.5
Body Mass Index (BMI)		
18.5-24.9 kg/m2(normal weight)	129	25.0
25-29.9 kg/m2(overweight)	198	32.7
≥ 30 kg/m2(obese)	256	42.3
Income Status		
$500 or less	195	32.2
$501-1000	375	62.0
$1001 or more	35	5.8
Parity		
0	9	1.5
1	114	18.8
2	153	25.3
3 or more	329	54.4
Place of Delivery		
House	94	17.1
Hospital	316	52.2
Both	186	30.7
Type of Delivery		
Vaginal	432	71.4
Cesarean section	54	8.9
Both	36	32.7
Oxytocin Induction (yes)	248	40.8
Episiotomy (yes)	296	48.9
Fetus over 4000 g (yes)	172	28.4
Chronic Disease (yes)	337	55.7
Chronic Constipation (yes)	251	41.5
Gynecological Surgery (yes)	190	31.4

Table 2: Information on women's menopausal period, UI and POP symptoms

Characteristics	n	%
Menopause Duration		
0-5 years	329	54.4
6-10 years	76	12.5
>11 years	200	31.1
Hormone Therapy		
Yes	115	19.0
No	490	81.0
Daily Urination		
≤ 6	396	65.5
> 6	209	34.5
Enuresis		
Yes	163	26.9
No	442	73.1
Nocturia		
Yes	404	66.8
No	201	33.2
Urinary Incontinence		
Yes	261	43.1
No	344	56.9
Urinary Incontinence Duration		
≤ 5	251	96.2
> 6	10	3.8
The frequency of Urinary Incontinence		
1/day	89	34.3
>1/day	64	24.5
<1/week	49	18.7
1/week	37	14.1
>1/week	22	8.4
Types of Urinary Incontinence		
Stress UI	75	28.8
Urge UI	62	23.7
Mixed UI	124	47.5
Intensity of Incontinence		
A few drops	144	55.1
Wetting the underwear	80	30.6
Wetting the clothes	28	10.7
Wetting the floor	9	3.6
Vaginal Prolapse		
Yes	147	24.3
No	458	75.7
Vaginal Bulging		
Yes	99	16.4
No	506	83.6

Table 3: Comparison of PISQ-12 Scale scores and general health conditions and obstetric data of women in terms of UI and POP

Characteristics	UI						POP					
	Yes		No				Yes		No			
	X̄ ±SD	Min.-Max.	X̄ ±SD	Min.-Max.	*ZMWU	**p	X̄ ±SD	Min.-Max.	X̄ ±SD	Min.-Max.	*ZMWU	**p
PISQ-12 Scale (Sub-Dimensions)	**28.41 ±3.25**	**20-36**	**30.20 ±3.51**	**22-38**	**-4.798**	**0.008**	**28.17 ±3.03**	**20-36**	**29.84 ±3.56**	20-38	**-4.152**	**0.000**
(behavioral-emotional factors)	6.13 ±2.25	4-11	6.88 ±2.90	4-13	-2.659	**0.008**	6.17 ±2.36	4-12	6.68 ±2.74	4-13	-1.898	0.058
(physical factors)	18.06 ±2.47	10-20	18.73 ±1.67	13-20	-2.634	**0.008**	17.17 ±2.42	12-20	18.85 ±1.77	10-20	-7.786	**0.000**
(Partner-relationship factors)	4.21 ±1.58	3-9	4.58 ±1.56	3-9	-3.491	**0.000**	4.82 ±1.88	3-9	4.29 ±1.45	3-9	-2.604	**0.009**

	UI							POP						
	Yes		No					Yes		No				
	n	%	n	%	*χ^2	**p	***OR (95% CI)	n	%	n	%	*χ^2	**p	***OR (95% CI)
BMI					6.814	**0.009**	0.60 (0.41-0.88)					11.644	**0.001**	0.43 (0.26-0.70)
≤ 25 kg/m2	55	34.4	105	65.6				23	14.4	137	85.6			
>25 kg/m2	206	46.3	293	53.7				124	27.9	321	72.1			
Constipation					60.582	**0.000**	3.19 (2.68-5.31)					60.582	**0.000**	1.34 (0.92-1.95)
Yes	155	61.8	96	38.2				69	27.5	182	72.5			
No	106	29.9	248	70.1				78	22.0	276	78			
Gynecological Surgery					18.067	**0.000**	2.11 (1.49-3.00)					42.275	**0.000**	2.46 (2.37-5.14)
Yes	106	55.8	84	44.2				78	41.1	112	58.9			
No	155	37.3	260	62.7				69	16.6	346	83.4			
Parity					6.96	**0.008**	0.65 (0.30-0.84)					3.459	0.063	0.62 (0.29-1.03)
0-1	24	29.06	57	70.4				13	16.0	68	84.0			
2 or more	237	45.2	287	54.8				134	25.6	390	74.4			
Type of Delivery					41.182	**0.000**	1.03 (0.07-0.16)					35.785	**0.000**	2.36 (0.08-0.16)
Vaginal	218	50.5	214	49.5				133	30.8	299	69.2			
Cesarean section	7	13.0	47	87				7	13.0	47	87			
Both	36	32.7	74	67.3				7	6.4	103	93.6			

Table 3: Continued

Episiotomy					8.444	**0.004**	1.08 (0.44-0.85)					8.006	**0.005**	0.58 (0.39-0.84)
Yes	110	37.2	186	62.8				57	19.3	239	80.7			
No	151	48.9	158	51.1				90	29.1	219	70.9			
Fetus over 4000 g					0.478	0.489	1.01 (0.79-1.61)					2.295	0.130	1.36 (0.91-2.03)
Yes	78	45.3	94	54.7				49	28.5	123	71.5			
No	183	42.3	250	57.7				98	22.6	335	77.4			
Characteristics	**UI**							**POP**						
	Yes		**No**					**Yes**		**No**				
	$\bar{X}$ ±SD	**Min.-Max.**	**$\bar{X}$ ±SD**	**Min.-Max.**	***ZMWU**	****p**		**$\bar{X}$ ±SD**	**Min.-Max.**	**$\bar{X}$ ±(SD)**	**Min.-Max.**	***ZMWU**	****p**	
Oxytocin Induction					16.820	**0.000**	0.49 (0.35-0.69)					9.540	**0.002**	0.53 (0.36-0.79)
Yes	82	33.2	165	66.8				44	17.8	203	82.2			
No	179	50	179	50				103	28.8	255	71.2			
HT					1.378	**0.240**	1.01 (0.51-1.18)					1.378	0.24	0.69 (0.41-1.14)
Yes	44	38.3	71	61.7				22	19.1	93	80.9			
No	217	44.3	273	55.7				125	25.5	365	74.5			
Enuresis					48.607	**0.000**	1.03 (2.53-5.42)					0.593	0.441	0.87 (0.55-1.29)
Yes	108	66.3	55	33.7				36	22.1	127	77.9			
No	153	34.6	289	65.4				111	25.7	331	74.9			
POP					49.029	**0.000**	3.19 (2.61-5.83)	---	---	---	---			
Yes	100	68.8	47	32.8				---	---	---	---			
No	161	35.2	297	64.8				---	---	---	---			

*ZMWU= Mann Whitney U *χ^2 Chi-square **p=0<0.05 ***OR: Odds Ratio UI: Urinary Incontinence POP: Pelvic Organ Prolapse

who were not given oxytocin induction (χ^2=16.820, p=0.000). UI was observed more frequently in women with a history of enuresis (χ^2=48.620, p=0.000), (Table 3).

When the POP data was examined, there was no significant difference found in terms of the number of deliveries (χ^2=1.328, p=0.240). When the type of delivery was examined, more POP symptoms were observed in vaginal deliveries (χ^2=35.785, p=0.000). More POP symptoms were observed in women who did not undergo episiotomy (χ^2=8.006, p=0.005) during labor and who were not given oxytocin induction (χ^2=9.540, p=0.002). There was no statistically significant difference between women with and without POP in terms of HT status (χ^2=1.378, p=0.240) and the presence of a fetus over 4000 g (χ^2=2.295, p=0.130). Women who had a body mass index > 25 (χ^2=11.644, p=0.001), had chronic constipation (χ^2=60.582, p=0.000), and had a gynecological surgery (χ^2=42.275, p=0.000) were found to have more POP symptoms (Table 3).

DISCUSSION

The climacteric period, which begins with the reduction of follicular function of the ovaries, is a period that lasts about 20 years until the age of 65 and is accepted as the onset of aging (12). The climacteric period is staged as premenopausal, menopausal and postmenopausal periods. The postmenopausal period includes a process of 8-10 years after menopause (13). While the age of menopause is between approximately 45-55 years of age in the world, it is stated as between 45-47 years of age in Turkey (9,13). Most of the women in this study were found to be in the postmenopausal period (66.9%).

Pelvic floor muscles are extremely sensitive to estrogen. In the postmenopausal period, estrogen decreases significantly, resulting in loss of elasticity and tonus in the pelvic floor muscles and connective tissue. Consequently, physical problems such as POP and UI are observed due to the pelvic floor dysfunction (14). UI is one of the most frequent problems observed in the postmenopausal period (15). Dellu et al. (4), in their study, reported that 47.3% of 1200 women who were in the climacteric period were found to have UI and the most frequently observed (19.2%) was mixed UI. In a study conducted by Şentürk and Kara (16) with 216 women in the postmenopausal period, the prevalence of UI was 45.3%. The most frequent type of incontinence was mixed UI with 64.3%. Şensoy et al. (17), in their study, found that 60.9% of menopausal women had UI. The results of this study, similar to other studies, demonstrated that UI is frequently observed in women in the postmenopausal period (43.1%). When the UI experiences of the women were examined , it was found that 28.8% of the patients had stress UI, 23.7% had urge UI and 47.5% had the symptoms of mixed UI.

In this study, a significant relationship was found between UI and factors such as multiparity, vaginal birth, chronic constipation, body mass index>25 (obesity), and history of gynecological surgery. Since the presence of chronic constipation and obesity causes an increase in factors such as intraabdominal and intravesical pressure and stress in the pelvic floor muscles, they increase the incidence of UI (4). In addition to high body mass index and the presence of chronic constipation, Cerruto et al. (18) reported that UI risk factors include the type of delivery (vaginal), the presence of POP, smoking, urinary infection, and gynecological surgery history. The tension in the pelvic floor muscles, pudendal nerve damage and ruptures in the perineal muscles due to pregnancy and vaginal delivery lead to UI (10). Biswas et al. (19) reported that more UI symptoms are observed in multiparous women and women who had a vaginal delivery. According to a study conducted by Aniulienė et al. (20), UI is seen more frequently in women who had a vaginal delivery and had more than two pregnancies, gave birth to a 3000 g or above newborn, and had perineal rupture during labor. In this study, more UI was observed in women who did not receive oxytocin induction and did not undergo episiotomy during delivery. Labor duration lasting more than 24 hours and spontaneous perineal lacerations increase the frequency of UI both in the postpartum period and at later ages (21). Within the scope of this study, it can be said that the presence of more UI in women was due to not receiving oxytocin induction or episiotomy. According to the Royal College of Obstetricians and Gynaecologists (RCOG) (22), similarly, episiotomy is effective in the presence of risk factors (rigid perineum, large fetus, fetal distress, etc.), when applied at the right time and the right angle (mediolateral) (Evidence level II). In the literature, there are different findings on episiotomy. In a study carried out by Kılıç (23), women with episiotomy have been reported to have more incidents of UI. In addition, in this study, there was more UI observed in women with enuresis in their childhood. Although Enuresis, defined as urinary incontinence during sleep in childhood, ceases in the progression of age, 2-3% of cases are experienced in future life (24). Therefore, as suggested in this study, it can be said that women who have enuresis in childhood have a higher risk of developing UI in their adulthood and that enuresis should be considered as a risk factor in women for UI.

Pelvic organ prolapse is another frequently observed pelvic floor disorder that profoundly affects the lives of women (14). In the study conducted by Slieker-ten Hove et al. (25), 21% of Dutch women between 45-85 years of age have been reported to have POP. According to a study carried out by Yıldız et al. (26), the prevalence of stage 2 and above of POP was 26.2% in menopausal women. In their study, Jennifer et al. (27) predict that by 2050, the frequency of POP is expected to increase by 46%, from 3.3 million to 4.9 million, due to the increased life expectancy and the increase in the elderly population. Similar to the findings of the literature, 24.3% of women had vaginal prolapse and 16.4% of them had vaginal bulging in this study.

Various risk factors were identified, which are thought to result in POP. High body mass index (> 25 = obesity), type of delivery (vaginal birth), multiparity, overweight (4000 g and over) infant delivery, and chronic constipation are some of these factors (28). As within the case of UI, POP is also affected by factors such as intraabdominal pressure, tension and tearing in the pelvic floor muscles. Accordingly, obesity, vaginal birth, chronic constipation and multiparity increase the incidence of POP

(21). In their study, Masenga et al. (29) found that POP is seen more frequently in multiparous women, in women who have chronic constipation and have a body mass index >25 and had a delivery over 4000 g. In a study conducted by Elbiss et al. (30), the presence of chronic constipation and a high body mass index were identified as POP risk factors. In this study, POP was seen more in multiparous women, those with vaginal delivery, chronic constipation, and those with a high body mass index (> 25). There was also a higher rate of POP in women who did not undergo episiotomy. It can be argued that POP occurs due to the inability to prevent pelvic lacerations which result from the absence of episiotomy applications when needed. Spontaneous pelvic lacerations have been reported to increase the likelihood of POP (31).

Another function of the pelvic floor muscles is to support the pelvic organs and prevent urinary incontinence, as well as to enable sexual intercourse. (32). Therefore, the presence of pelvic floor dysfunction negatively affects sexual function. In the presence of POP and UI, which are the most common symptoms of pelvic floor dysfunction, women stay away from sexual life due to vaginal obstruction, not feeling attractive, fear of incontinence during intercourse, and an inability to orgasm (33,34). According to a study conducted by Güdücü and Özcan (15), women with UI complaints had lower PISQ-12 scale scores than those who did not have such complaints. In the study of Li-Yun-Fong et al. (35), women with POP were found more likely to have symptoms of sexual dysfunction, such as sexual reluctance and lack of orgasm. According to a study conducted by Novi et al. (36), 56% of POP patients experience urinary incontinence and 13% of them have fecal incontinence and very seldom have intercourse. It is also reported that, in the same study, 70 % of them abstained from sexual intercourse due to the fear of urinary or fecal incontinence although they did not have a low sex drive. In a study carried out by Çayan et al. (37), urinary incontinence was observed more frequently in women with sexual dysfunction. Similarly, in a study by Turhan et al. (38), urinary incontinence was found to be a risk factor for sexual dysfunction. According to the PISQ-12 scale scores in this study, women with POP and UI were found to have poorer sexual function. When the physical factor sub-dimension, which questions the effects of prolapse and incontinence on sexual function, was examined, it was found that sexual function was affected more in women with POP and UI. Of the women with UI, 78.2% responded 'always' to the question of whether they had urinary incontinence during sexual intercourse. Of women with POP, 69.4% stated that they abstain from sexual intercourse due to the reasons such as protrusion, palpable mass and bulging in their vagina. As stated in the literature as well as in this study, it is seen that sexual function is poorer in women with UI and POP.

CONCLUSION

According to the results of the study, the prevalence of UI and POP in the menopausal period was found to be considerably high. The identified UI and POP risk factors are as follows: High body mass index, constipation, vaginal delivery, the presence of POP, smoking, urinary infection, and gynecological surgery history. It was found that sexual function was adversely affected in women with POP and UI. Considering that women spend 1/3 of their lives in the postmenopausal period, risk assessment, treatment and solution of sexual problems pertaining to POP and UI will contribute to the improvement of their quality of life.

The results of the study are important in terms of increasing the awareness of healthcare professionals about urinary incontinence and pelvic organ prolapse, which are common in the postmenopausal period, and informing women to prevent these diseases. The prevalence of urinary incontinence and pelvic organ prolapse in postmenopausal women was quite high. Moreover, postmenopausal women with urinary incontinence and pelvic organ prolapse had worse sexual function. In addition, it can be a resource for health professionals on sexual dysfunction, which may occur due to these diseases and significantly affect women's quality of life, and should not be ignored.

Ethics Committee Approval: This study was approved by the ethics committee of Zeynep Kamil Gynecology and Pediatric Training and Research Hospital's Clinical Research Ethics Committee (Decree no: 38; Date: 03.07.2018).

Informed Consent: Written consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- M.T., Ü.Y.Ö., Ö.Ö.; Data Acquisition- M.T., Ö.Ö.; Data Analysis/Interpretation- M.T.; Drafting Manuscript- M.T., Ü.Y.Ö., Ö.Ö.; Critical Revision of Manuscript- M.T., Ü.Y.Ö.; Final Approval and Accountability- M.T., Ü.Y.Ö., Ö.Ö.

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