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Associated Factors Causing Uterine Prolapse in Nongeriatric and Geriatric Female Patient Populations and Analysis of Pathological Diagnoses

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ABSTRACT

Objective: Many factors influence the etiology of uterine prolapse (UP). This study, therefore, analyzed factors affecting UP in nongeriatric and geriatric age groups.

Materials and Methods: The 494 patients included in the study were divided into two groups: 317 nongeriatric patients (aged <65; 64.2%) and 177 geriatric patients (aged ≥65; 38.8%). Factors affecting UP were analyzed.

Results: Multivariate logistic regression analysis indicated that in all patients, the number of births (odds ratio [OR]=1.254; 95% confidence interval [CI]=1.081–1.456; p=0.003) and menopause (OR=2.159; 95% CI=5.612–4.334; p=0.031) increased the risk of UP. Receiver operating characteristic (ROC) analysis also indicated that the cutoff point for the number of births in all patients was >3 (area under the curve [AUC]=0.553; 95% CI=0.508–0.597; p=0.037). Although the AUC value (AUC=0.635) calculated for the number of births in patients aged ≥65 was higher than those calculated for body mass index and the number of miscarriages (AUC=0.582 and AUC=0.583, respectively), this difference was not statistically significant (p>0.05).

Conclusion: UP is closely related to the number of births and the presence of menopause. Although no significant correlation was found between age at menopause and the number of births in patients aged <65, a statistically significant positive correlation was found between age at menopause and the number of births in patients aged ≥65.

Keywords: Geriatrics, uterine prolapse, birth, menopause, body mass index, risk factors

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INTRODUCTION

Pelvic organ prolapse (POP) is the descent of one or more of the anterior vaginal wall, posterior vaginal wall, uterus, cervix, or the apex of the vagina. Uterine prolapse (UP) is the protrusion of the uterus through the vaginal opening (1). Patients often present with symptoms such as a feeling of heaviness in the genital area or a mass protruding from the vagina. The incidence of UP is 3%–11% in USA (2). UP is an important cause of morbidity and mortality among women in countries with low socioeconomic status (3). However, in developed countries, mortality and morbidity rates are lower. UP is associated with the quality of life caused by various factors such as physical health, emotional stress, and social status (4). In addition to the mechanical disorders it creates, UP is an important social health problem that can negatively affect sexual life, body perceptions, and the quality of life. For UP to occur, the uterosacral ligaments of the pelvic fascia must lose their elasticity. This is related to the aging of these structures and to excessive mechanical causes (5). Many factors are held responsible for the etiology of UP. The number of births, advanced age, and obesity are the most common risk factors for UP development. However, other important risk factors are increased intra-abdominal pressure, constipation, tissue atrophy due to aging, menopause, and congenital ligament weakness, high-birth-weight babies, prolonged second stage of labor, and giving birth before the age of 25 (6). Still, UP can also be seen in women who have never given birth (7). The extant literature reports that comorbidities, such as hypertension (HT) and diabetes mellitus (DM), increase urinary incontinence and POP (1). Given this background, the present study analyzes risk factors affecting UP and the pathological results of UP operations among women in geriatric and nongeriatric age groups.

MATERIALS and METHODS

Study Population

After obtaining approval from the Institutional Ethics Committee (Date of Approval/Protocol No: 03.07.2020–3/10), the study was designed as a single-center, retrospective descriptive study. Seven hundred ninety-eight patients who applied to our hospital with UP between January 2010 and June 2020 were included in the study. Patient information was reached by scanning the files in the hospital's electronic patient data system (SARUS DBMS, ESS Ltd Şti, Ankara, Turkey) and archive system. One hundred and six

patients were excluded because their files were not accessible. Fifteen patients with other pelvic organ prolapse and 183 patients under the pelvic organ prolapse quantification (POP-Q) system stage IV were excluded from the study. Electronic patient records and archive information were available for the remaining 494 patients who included the study. The average age of the patients was calculated to be 60.6±8.6 years. Among those patients, 317 (64.2%) patients were aged <65 years, and 177 (38.8%) patients were aged ≥65 (Fig. 1).

Assessments

We define 65 years and older as the geriatric age group (8). According to our study aim, 494 sampled patients were divided into two groups: nongeriatric (aged 18–64) and geriatric (aged ≥65). In both groups, body mass index (BMI) [(Healthy: 18.5–24.99 kg/mI, overweight: ≥25.00 kg/mI, obese: ≥30.00 kg/mI, and severely obese: ≥40.00 kg/mI)] (9), number of deliveries, type of delivery, number of miscarriages, presence of menopause, age at menopause, presence of HT, and presence of DM were evaluated through logistic regression analysis to determine their effects on UP. Pelvic organ prolapse was staged with POP-Q, according to this staging system: Stage 0: No prolapse is demonstrated. Stage I: The most distal portion of the prolapse is more than 1 cm above the level of the hymen. Stage II: The most distal portion of the prolapse is situated between 1 cm above the hymen and 1 cm below the hymen. Stage III: The most distal portion of the prolapse is more than 1 cm beyond the plane of the hymen but everted at least 2 cm less than the total vaginal length. Stage IV: There is complete eversion or eversion at least within 2 cm of the total length of the lower genital tract (10). The cutoff point for our study participants was POP-Q stage IV. Stage III and below were excluded from the study.

Statistical Analysis

The statistical analysis was performed using the Statistical Package for the Social Sciences for Windows, version 23.0 (IBM Corporation, Armonk, NY, USA). The normality assumptions were controlled by using the Shapiro–Wilk test. Descriptive analyzes were presented using mean±SD (range), median (range), or n (%), where appropriate. Categorical data were analyzed using the Pearson chi-squared and Fisher's exact tests. The differences between the two groups were evaluated using the Mann–Whitney U test for non-normally distributed data, whereas Student's t test was used for normally distributed data. The receiver operating characteristic (ROC) curve analysis was applied to evaluate the predictive performance of age at menopause, BMI, and number of births and miscarriages; the area under the curve (AUC), sensitivity, and specificity were calculated and reported with 95% confidence intervals (CIs). The optimal cutoff point for measurements was determined as the value of the maximum Youden Index. The Spearman correlation coefficient was applied to investigate the correlation between continuous variables. Multivariate logistic regression analysis was used to determine independent risk factors associated with prolapse. Variables with p<0.1 in the univariate analysis were further tested in the multivariate model. A p-value <0.05 was considered to indicate statistical significance. The adequacy of the sample size was done with G power, and the power was over 80% for a type 1 error of 5%. Based on the research of Isık et al. (1), the effect size was determined as d=0.532.

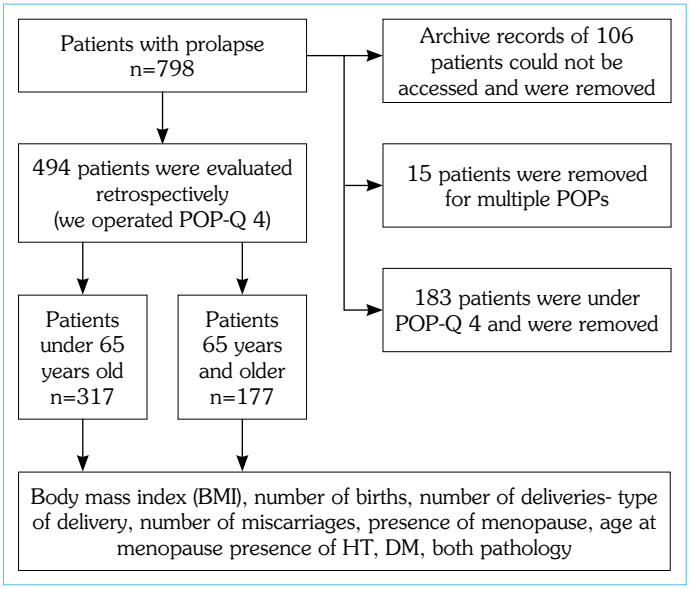

Figure 1. Retrospective flowchart

RESULTS

The average age of patients was 60.6±8.6 years. Three hundred seventeen (64.2%) patients were aged <65 and 177 (38.8%) patients were aged ≥65. The mean ages of the patients aged <65 and ≥65 were 55.5±5.3 and 69.8±5.1 years, respectively. 93.9% of patients had vaginal deliveries, 4% had cesarean deliveries, and 2.1% had vaginal + cesarean deliveries. The median number of deliveries in patients was three (range: 0–10), whereas the median number of miscarriages was one (range: 0–8). DM was observed in 49 (9.9%) patients; HT, in 65 (13.2%) patients; and both, in 63 (12.8%) patients. Concerning comorbid pathologies, chronic cervicitis + atrophic endometrium exhibited the highest rate, being found in 64 patients (26.2%), and endometroid adenocarcinoma had the lowest rate, being found in one patient (0.4%) (Table 1). No statistically significant difference was found in terms of BMI (p=0.615) and comorbid diseases (p=0.642) based on age. The vaginal delivery rate, which was 97.7%, among those aged ≥65, was statistically higher than that among those aged <65 (91.8%) (p=0.026). The median number of deliveries and the number of miscarriages were higher in patients aged ≥65 (p<0.001). All patients aged ≥65 were in menopause (100%), whereas 86.1% of patients <65 were in menopause (p=0.001). The average age at menopause in patients aged <65 was 48.1±4.2 years, whereas that of patients aged ≥65 was 50.9±4.7 (p=0.001). When the patients' pathology findings were analyzed based on age group, it was determined that the prevalence rate of chronic cervicitis + basal endometrium was 11.9% (19 patients) among those aged <65 (p=0.004) and that the prevalence rate of chronic cervicitis + senile cystic hyperplasia was higher in patients aged ≥65 (10.6%; 9 patients) (p<0.001). No significant differences were observed in other pathological findings based on age group (p<0.05) (Table 1). The multivariate logistic regression analysis indicated that the number of births (odds ratio (OR)=1.254; 95% CI=1.081–1.456; p=0.003) and menopause (OR=2.159; 95% CI=5.612–4.342; p=0.031) increased the risk of UP in all patients (Table 2).

In patients aged <65, menopause (OR=2.553; 95% CI=1.253–5.199; p=0.010) was an independent risk factor for UP. In pa-

Table 1. Patients' characteristics

Variables	Total (n=494)	<65 (n=317)	≥65 (n=177)	p
Age (years)	60.6±8.6 (43–88)	55.5±5.3 (43–64)	69.8±5.1 (65–88)	<**0.001**
BMI	25.7 (16.9–59.1)	25.7 (16.9–59.1)	25.4 (19.1–39.7)	0.615
Type of delivery				0.026
Vaginal	464 (93.9)	291 (91.8)[a]	173 (97.7)[b]	
Cesarean	20 (4)	18 (5.7)[a]	2 (1.1)[b]	
Vaginal + Cesarean	10 (2.1)	8 (2.5)[a]	2 (1.1)[a]	
Number of deliveries	3 (0–10)	3 (0–9)	4 (0–10)	<**0.001**
Number of miscarriages	1 (0–8)	1 (0–8) Mean: 1.15	1 (0–7) Mean: 1.48	**0.001**
Menopause				<**0.001**
No	44 (8.9)	44 (13.9)	0 (0)	
Yes	350 (91.1)	273 (86.1)	177 (100)	
Age at menopause (years)	49.2±4.6 (40–60)	48.1±4.2 (40–60)	50.9±4.7 (40–60)	<**0.001**
Comorbid diseases				0.642
No	317 (64.2)	210 (66.2)	107 (60.5)	
DM	49 (9.9)	30 (9.5)	19 (10.7)	
HT	65 (13.2)	39 (12.3)	26 (14.7)	
DM + HT	63 (12.8)	38 (12%)	25 (14.1)	
Pathology				
Chronic cervicitis + atrophic endometrium	64 (26.2)	36 (22.6)	28 (32.9)	0.082
Chronic cervicitis + basal endometrium	20 (8.2)	19 (11.9)	1 (1.2)	**0.004**
Chronic cervicitis + endometrial polyp	31 (12.7)	23 (14.5)	8(9.4)	0.256
Chronic cervicitis + adenomyosis	41 (16.8)	29 (18.2%)	12 (14.1)	0.415
Chronic cervicitis + senile cystic hyperplasia	9 (3.7)	0 (0)	9 (10.6)	<**0.001**
Cervical erosion + atrophic endometrium	10 (4.1)	5 (3.1)	5 (5.9)	0.293
Chronic cervicitis + myoma	34 (13.9)	22 (13.8)	12 (14.1)	0.949
Chronic cervicitis CIN1 + atrophic endometrium	3 (1.2)	1 (0.6)	2 (2.4)	0.225
Squamous hyperplasia + adenomyosis	26 (10.7)	18 (11.3)	8 (9.4)	0.647
Chronic cervicitis + chronic endometritis	5 (2)	5 (3.1)	0 (0)	0.102
Endometroid adenocarcinoma	1 (0.4)	1 (0.6)	0 (0)	0.475

Student's t test; Mann–Whitney U test; Pearson's chi-squared test. Data are presented as n (%), mean±SD (range), or median (range). Different lowercase letters in a row indicate a statistically significant difference between groups. DM: Diabetes mellitus; HT: Hypertension

Table 2. Multivariate logistic regression analysis for determining the risk factors associated with pelvic organ prolapse in age groups

	Total		<65		≥65	
Variables	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age (years)	0.978 (0.954–1.002)	0.077	0.96 (0.916–1.006)	0.090	1.03 (0.962–1.103)	0.391
BMI	0.965 (0.928–1.003)	0.073	0.985 (0.941 to 1.03)	0.505	0.918 (0.846–0.996)	0.040
Number of deliveries	1.254 (1.081–1.456)	**0.003**	1.079 (0.888–1.312)	0.444	1.563 (1.21 to 2.019)	0.001
Number of miscarriages	0.869 (0.74 to 1.02)	0.085	1.067 (0.875–1.301)	0.523	0.588 (0.427–0.808)	**0.001**
Menopause	2.159 (1.074–4.342)	**0.031**	2.553 (1.253–5.199)	0.010	–	–

Variables with p<0.1 in univariate analysis were included in the multivariate model. OR: Odds ratio; CI: Confidence interval; BMI: Body mass index

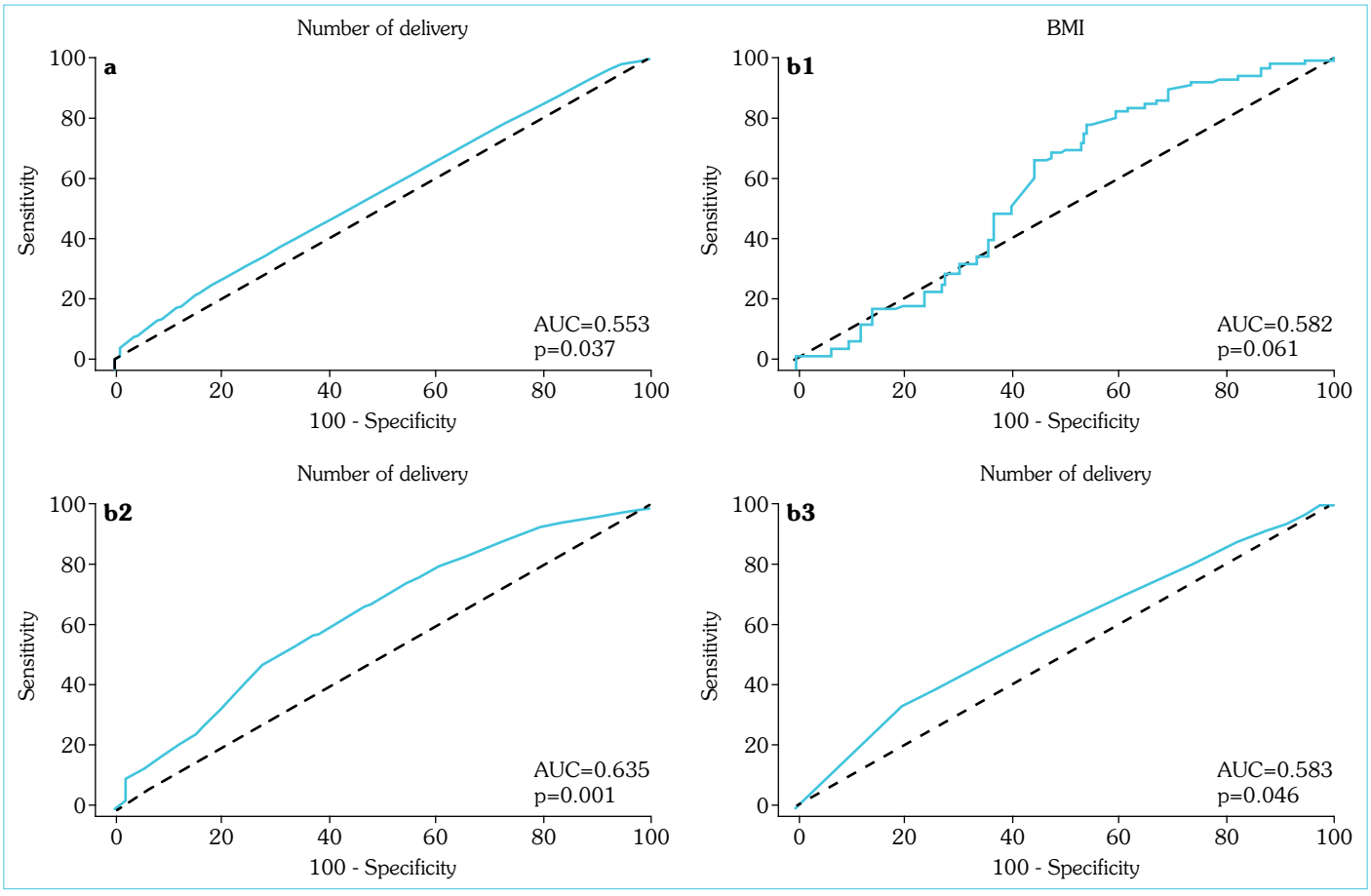

Figure 2. (a) Roc curve for number of delivery and age of menopause to the predict prolapse in all patients. (b) Roc curve for BMI, number of delivery, miscarriage and age of menopause to the predict prolapse in patients aged ≥65 years

tients aged ≥65, decreased BMI (OR=0.918; 95% CI=0.846–0.996; p=0.040), decreased number of miscarriages (OR=0.588; 95% CI=0.427–0.808; p=0.001), and increased number of births (OR=1.563; 95% CI=1.21–2.019; p=0.001) were independent risk factors for UP (Table 2).

The ROC analysis determined that for all patients, >3 births were the optimal cutoff point (AUC=0.553 (95% CI=0.508–0.597; p=0.037); sensitivity=49.59%; specificity=56.8%) (Fig. 2a). Although the AUC value (AUC=0.635) calculated for the number of births in patients aged ≥65 was higher than those calculated for BMI and the number of miscarriages (AUC=0.582 and AUC=0.583, respectively), this difference was not statistically significant (p>0.05).

In patients aged ≥65, the optimal cutoff points were as follows:

1 BMI: ≤27.099 kg/m^2 (AUC=0.582 (95% CI=0.505–0.655, p=0.061), sensitivity=77.65%, specificity=45.65%);

2 The number of births: >4 (AUC=0.635 (95% CI=0.560–0.706, p=0.001); sensitivity=48.24%; specificity=71.74%); and

3 The number of miscarriages: ≤1 (AUC=0.583 (95% CI=0.506–0.656, p=0.046); sensitivity=56.47%, specificity=55.43%) (Fig. 2b).

Although there was no significant correlation between age at menopause and number of births in patients aged <65 (p=0.813), a statistically significant positive correlation was found between age at menopause and the number of births in patients aged ≥65 (r=0.215, p=0.004). There was no statistically significant correlation between BMI and age at menopause in either age group (p>0.05) (Fig. 3).

DISCUSSION

UP is a very common disorder, especially among older women (11). Advanced age-related physical slowdown is an important risk factor for UP (12). Although this disease affects the geriatric age group, it can also be seen in younger groups with pelvic floor disorders (13). In this study, we used the logistic regression model to evaluate the effects of age, BMI, the number of births, the number of miscarriages, and the presence of menopause on UP. The number of births and menopause were found as risk factors in all patients. Although menopause was found to be an independent risk factor in the patient group under 65 years of age, a decrease in BMI and the number of miscarriages, and an increase in the number of births in the group over 65 were found to be independent risk factors (Table 2). Entering menopause at a younger age and being exposed to the damage caused by menopause to the female genital system for a longer period of time may make us think that it can facilitate the formation of UP. In this study, the number of miscarriages was found to be higher in the geriatric age group. This could be interpreted as suggesting that an increasing number of miscarriages may have an effect on the deformation of the ligaments holding the uterus in place. Although UP is associated with age and the number of births, it has also been found to be closely

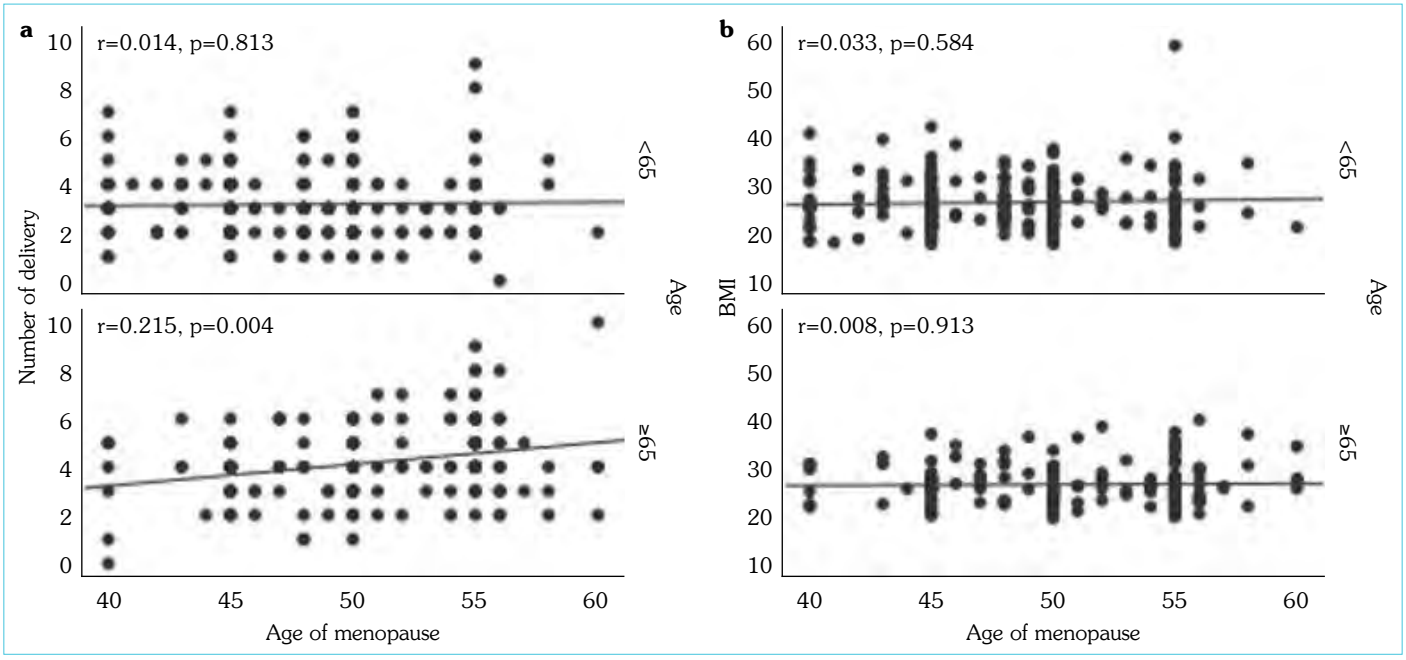

Figure 3. Correlation of number of delivery and BMI with age of menopause

related to both vaginal and cesarean deliveries (14). Previous studies have demonstrated that only the number of births affects UP, whereas there is no statistically significant difference between UP and comorbidity factors such as age, BMI, age at menopause, DM, and HT (15). Other pieces of extant literature have determined that an increased BMI is associated with early-onset menopause (16), but the present study found no statistically significant correlation between BMI and age at menopause in either age group. Although aging plays a complex role in the pathogenesis of POP (17), some research reports that age, parity, presence of menopause, and hormone replacement therapy are significantly associated with UP (18). In this study, a statistically significant relationship was found between menopause and UP, indicating that the risk increases in geriatric women who do not undergo any hormone replacement therapies during the postmenopausal period. Some previous studies reported that the number of births, medical miscarriage, and BMI do not affect age at menopause (19). In this study, no significant correlation was found between age at menopause and the number of births in patients aged <65, whereas a statistically significant positive correlation was found between age at menopause and the number of births in patients aged ≥65.

In gynecological oncology studies, uterine malignancies were confirmed at rates of 63.5% uterine, 17.5% ovarian, 10.2% cervical, 5.4% vulvar/vaginal, and 3.4% others (20). However, in this study, only one (0.4%) patient in the nongeriatric group was diagnosed with endometroid adenocarcinoma. It is noteworthy that the incidence of malignancies in women with UP is quite low. Chronic cervicitis + basal endometrium incidence in patients aged <65 [19 (11.9%)] is at a higher level than the incidence of chronic cervicitis + senile cystic hyperplasia in patients aged ≥65 [9 (10.6%)]. Our study has some limitations; the first is its retrospective nature, and the second is that some of the results of the study were not compatible with the literature. We think that this may be due to the limited number of patients.

CONCLUSION

It was observed that the effects of age, BMI, delivery mode, the number of abortions, menopausal age, and comorbidity factors on UP in women were limited. UP appears to be closely related to high birth rates and the presence of menopause. According to the results of our study, the risk of UP increases in women with more than three deliveries in both age groups. Although there was no significant relationship between the age at menopause and the number of births in patients under 65 years of age, a statistically significant and positive relationship was found between the age at menopause and the number of births in patients aged 65 and over. A larger randomized controlled trial, or at least a prospective cohort study, will be required to draw conclusions that are more definitive.

Ethics Committee Approval: The Antalya Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 03.07.2020, number: 10/3).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflict of interest to declare.

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