Menopause: The Journal of The North American Menopause Society
Vol. 27, No. 4, pp. 450-458
DOI: 10.1097/GME.0000000000001523

ORIGINAL STUDY

Pelvic floor disorders in women with premature ovarian insufficiency: a cross-sectional study

Júlia Ferreira Fante, PT, MsC, Helymar da Costa Machado, BS, Cassia Raquel Teatin Juliato, MD, PhD, Cristina Laguna Benetti-Pinto, MD, PhD, and Luiz Gustavo Oliveira Brito, MD, PhD

Abstract

Objectives: This study aimed to investigate the prevalence of self-reported main pelvic floor disorders (PFD) (urinary incontinence [UI], pelvic organ prolapse [POP], and fecal incontinence [FI]) and its associated factors in women with premature ovarian insufficiency (POI) and a control group.

Methods: This was a cross-sectional study wherein two groups were interviewed from August, 2017 to November, 2018—women with POI (n = 150) and a control group matched for age and body weight (n = 150). Sociodemographic variables and two questionnaires validated in Brazilian Portuguese language for PFD (Kings Health Questionnaire [KHQ] and Pelvic Floor Distress Inventory—20 [PFDI-20]) were used. Laycock's power, endurance, repetitions, fast contractions, every contraction timed (PERFECT) scale for pelvic floor muscle assessment was used in both groups.

Results: The prevalence of self-reported UI was 27.33% and 37.33% for POI and control groups ($P > 0.05$), respectively. There was no perceived difference regarding the prevalence of POP (9.33% POI group vs 8% control group; $P = 0.682$) and FI (8% POI vs 4% control group; $P = 0.145$). The P (power) ($P = 0.46$), E (endurance) ($P = 0.91$), R (repetitions) ($P = 0.88$), and F (fast contractions) ($P = 0.19$) values were statistically similar in both the groups. Multivariate analysis (n = 141) showed that higher weight (odds ratio [OR] 1.047 [1.018-1.076]; $P < 0.001$) and gravidity rates (OR 1.627 [1.169-2.266]; $P < 0.01$) were risk factors for UI and higher weight (OR 1.046 [1.010-1.084]; $P = 0.01$), and presence of comorbidities (OR 8.75 [1.07-71.44]; $P < 0.01$) were risk factors for POP in the POI group; there was no variable that was associated with FI.

Conclusions: Women with POI did not have significant differences when compared with the control group regarding the prevalence of PFD and pelvic floor muscle assessment. Having higher weight and gravidity rates were associated with self-reported UI, while the presence of comorbidities and higher weight were risk factors for POP in the POI group.

Key Words: Cross-sectional study – Fecal incontinence – Hormone therapy – Pelvic organ prolapse – Premature ovarian insufficiency – Urinary incontinence.

***Video Summary*:** http://links.lww.com/MENO/A555.

Premature ovarian insufficiency (POI) is defined as ovarian failure before 40 years of age. This dysfunction is characterized by the interruption or abnormal frequency of menstruation for at least 4 months, and an increase in follicle-stimulating hormone (FSH) and decrease in estradiol. POI can be classified into primary and secondary, but in most cases, it is nonidentifiable.[1] Clinical consequences from having POI are vasomotor symptoms, osteoporosis, genital atrophy (more recently named genitourinary syndrome of menopause), and a reduction in quality of life for many women.

The genital and urinary tract both respond to estrogen receptor activation. Thus, a decrease in the estrogen levels might cause vulvovaginal and urinary symptoms. Vaginal dryness, dyspareunia, stress urinary incontinence (UI), urgency, urgency incontinence, and nocturia may be referred.[2] Hormone therapy (HT) is indicated for women with POI, especially for vasomotor symptoms and for preventing bone loss.[1] A topical approach is used for treating genitourinary syndrome of menopause.[3]

The pelvic floor consists of suspension (ligaments and fascia) and support structures (pelvic and urogenital diaphragm

Received August 25, 2019; revised and accepted January 8, 2020.
From the Department of Obstetrics and Gynecology, School of Medical Sciences, University of Campinas, São Paulo, Brazil.
Ethical approval: Institutional Review Board, School of Medical Sciences, University of Campinas, CAAE 73266217.9.0000.5404.
Funding/support: Julia Fante received a research scholarship from Coordenação de Aperfeiçoamento de Pessoal Nível Superior (CAPES), code 001.
Financial disclosure/conflicts of interest: None reported.
Supplemental digital content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's Website (www.menopause.org).
Address correspondence to: Luiz Gustavo Oliveira Brito, MD, PhD, Rua Alexander Fleming, 101 Cidade Universitária, Barão Geraldo, Campinas 13083-881, Campinas, São Paulo, Brazil. E-mail: lgobrito@unicamp.br

composed of muscles), formed mainly by the levator ani muscle. This has three portions (puborectalis, pubococcygeus and iliococcygeus) and acts as support for the bladder, the reproductive organs, and the rectum. In this region, there are steroid hormone receptors (estrogen, progesterone, and testosterone)[4,5]; hence, the pelvic floor is susceptible to steroidal hormonal changes,[6] and its quality and proper functioning depend, in part, on the presence of these hormones.[7]

Age and hypoestrogenism are factors related to pelvic floor dysfunction. However, it is difficult to isolate both factors to understand which one has a greater influence. The main pelvic floor disorders (PFD) (UI, pelvic organ prolapse [POP], and fecal incontinence [FI]) are related to hypoestrogenism.[8-10] The International Continence Society (ICS) and International Urogynecological Association (IUGA) define UI and FI as any involuntary loss of urine, and solid or liquid stools, respectively. Meanwhile POP is defined as the loss of support for the uterus, bladder, and bowel leading to the descent of one or more of these organs into the vagina.[11] POI is thought to be an ideal model to analyze the association between hypoestrogenism and female PFD because it develops independently of age, at a younger age range; and without the effect of estrogen. Considering that women with POI are exposed to a chronic hypoestrogenic state, it is possible that they present with more PFD than women at the same age, even when using HT. Thus, we sought to assess the prevalence of PFD in women with POI and compare it with a control group, and also to determine risk factors.

METHODS

Study design, participants, and inclusion/exclusion criteria

A cross-sectional study was conducted in an outpatient clinic from a tertiary, academic hospital from August, 2017 to November, 2018. The Institutional Review Board approved this study. All principles described by the Helsinki Declaration[12] were followed, and women were given the informed consent to read and sign it if they agreed to participate.

A total of 300 participants were included and divided into two groups: POI (n = 150) and control group (n = 150). The diagnosis of POI was based on the European Society of Human Reproduction and Embryology guideline[1]: oligo/amenorrhea in the past 4 months and FSH levels higher than 25 IU/L under age <40 years (at diagnosis). The control group comprised of women who were at the Family Planning Clinic of the same institution and they were matched by age (range of 2 years), body mass index (BMI) (deviation of 3 kg/m^2), had regular menstrual cycles (24-38 days),[13] and did not use any hormonal medications; these women could use copper IUD, condoms, or undergo tubal ligation.

Exclusion criteria from the POI group were present or previous history of inferior genital tract cancer, previous treatment with pelvic radiotherapy, pregnant women, and previous urogynecological surgery (eg, sling, anterior/posterior colporrhaphy, Burch operation). The control group had the same exclusion criteria as mentioned above plus the use of any hormone (contraceptive) for at least 12 months. We had seven refusals to participate in the control group.

Variables and questionnaires

All women were interviewed with a standardized questionnaire containing sociodemographic variables. The Pelvic Floor Distress Inventory—20 (PFDI-20) and Kings Health Questionnaire (KHQ) validated for Brazilian Portuguese language[14,15] were given to the women to complete, and in case they had any questions, an interviewer was available to help them.

The following variables were analyzed: age, BMI, education level, race, tobacco use, position at work (standing, sitting), comorbidities, duration of menopause, age at POI diagnosis, time of POI diagnosis, gravidity and parity, number of vaginal deliveries and cesarean deliveries, presence of sexual activity, physical activity with impact on pelvic floor, karyotype analysis (for women with POI), HT use, duration using (or not using) HT, reasons for stopping HT, type of HT, total time using HT, and presence of self-reported symptoms of UI, POP, and FI.

All women were invited to undergo a pelvic floor muscle assessment by vaginal palpation using the power, endurance, repetitions, fast contractions, every contraction timed (PERFECT) scale and grading of each variable with the modified Oxford scale. Before starting the evaluation, the physical therapist briefly explained to the participants the anatomy and function of the pelvic floor muscles, and explained their importance. Women were positioned with their hips abducted, flexed knees, and feet supported on the stretcher. Thus, the examiner would ask women to voluntarily contract their pelvic muscles, and observed whether there was a visible contraction. Then, the examiner, wearing gloves that were superficially covered with lubricant, would perform a digital palpation, and moderate pressure was applied to the muscle to help in performing an appropriate contraction. This was repeated and the assessment was performed.

The PFDI-20 presents three subscales: Pelvic Organ Prolapse Distress Inventory (POPDI-6), Colorectal-Anal Distress Inventory (CRADI-8), and Urinary Distress Inventory (UDI-6). Each question started with a yes/no answer. Subsequently, if the answer was positive, they were asked for quantification of the symptoms in a Likert scale format. Each subscale presented a mean score multiplied by 25 (0-100), and the total sum would vary from 0 to 300.[14] The KHQ was composed of 21 questions divided into eight domains (general health perception, impact of UI, limitation for daily activities, physical and social limitations, personal relationship, emotions, and sleep/disposition). This questionnaire was scored according to each domain.[15]

Statistical analysis

We used SAS statistical package to perform the analysis (version 9.2, SAS Institute, Cary, NC).[16] Categorical variables were analyzed by chi-square or Fisher's test, and continuous variables by Mann-Whitney test. To correlate the

numerical scales that were used in this study, Spearman's correlation test was used. For each self-reported pelvic floor dysfunction (UI, FI, and POP), we used logistic regression with univariate and multivariate analysis with stepwise criteria for selecting the variables. The adopted significance level was 5%.

For the sampling size calculation, given that UI prevalence in a young population is 15% and there is no information regarding the general UI prevalence in women with POI, considering a 10% difference in the proportion between the groups, a 80% study power, and a 5% significance level, a sampling size of 113 women was calculated, with a 1:1 ratio for the control group.

RESULTS

Baseline characteristics of the groups

Three hundred women were recruited and divided into two groups (n = 150, POI group; n = 150, control group), and they were matched for age ($P = 0.187$) and BMI ($P = 0.069$). In summary, the women presented with a mean age of 34.30 (±8.58), BMI of 26.85 kg/m^2 (±5.16), with 9 to 11 years of education (47.83%), white (50.67%), not using tobacco (92.67%), and with no comorbidity (49.33%). Forty six per cent of women were nulliparous (n = 138) and 82.67% reported sexual activity. Most of the women conducted their work activity in a standing position (66.67%) and did not perform medium/high-impact physical activity (86%). Regarding PFD, 32.33% self-reported UI, 6% reported FI, and 8.67% POP. Of the women with POI, 18.67% presented with karyotype alteration.

Table 1 shows baseline characteristics between women with POI and control women. It was observed that there was a higher percentage of comorbidities in the POI group (61.33%; $P < 0.001$), rate of secondary amenorrhea, and HT use.

Prevalence of pelvic floor dysfunction between POI and control groups

No statistically significant differences were perceived between the groups regarding the prevalence of PFD. Women with POI presented a 27.33% prevalence of UI, 9.33% of POP, and 8% of FI when compared with the control group (37.33% for UI, 8% for POP, and 4% for FI; $P > 0.05$). Control women with UI reported a higher impact on their quality of life when compared with women with POI (21.33%; $P = 0.03$) (Table 1). When we analyzed women with POI, and compared the prevalence of PFD within this group, the UI prevalence was higher in women who were not using HT (41.67%) versus 22.81% of women with POI using HT ($P = 0.03$). The prevalence of POP was 7.89% and 13.89% for women using and not using HT ($P > 0.05$), and prevalence of FI was 6.14% and 13.89% for women using and not using HT ($P > 0.05$).

Pelvic floor muscle assessment

A higher prevalence of grade 2 force (range 0-5) was found when using the PERFECT scale. The P component also had grade 2 in both groups (42.86% POI and 46.59% control) with no significant difference (Table 2). The groups did not present with any difference with respect to endurance, repetitions, and fast contractions ($P > 0.05$) (Table 3). Among women with POI, there was a high grade 3 (37.25%) and grade 2 (63.16%) in the P component in women who used HT when compared with women who did not use HT.

Questionnaires and the results between POI and control women

Regarding the PFDI-20 questionnaire, we did not find any difference among the domains, except for the POPDI questionnaire, with a higher score in the control group (7.25 ± 10.87; $P = 0.01$) versus the POI group (5.03 ± 9.46). Regarding the KHQ, all subscales were homogeneous between the groups, except for the emotion subscale, which presented a higher score in the control group (6.37 ± 18.54 vs 5.63 ± 20.75—POI; $P = 0.04$) (Table 2).

Among women with POI, the PFDI-20 total score was statistically significantly higher in the group not using HT (38.28 ± 41.07; $P = 0.03$) versus women using HT (22.55 ± 35.26). The KHQ presented statistically significant differences for women with POI not using HT in the subscale of social limitations (6.02 ± 15.79 vs 2.14 ± 10.31; $P = 0.03$), personal relations (8.33 ± 20.68 vs 2.56 ± 12.33; $P = 0.03$), severity (19.44 ± 26.50 vs 7.89 ± 13.75; $P = 0.02$), and sexual intercourse (0.19 ± 0.52 vs 0.05 ± 0.35; $P = 0.01$).

Among women with POI, a higher mean age at diagnosis was associated with UI ($P < 0.01$), and also not using HT and higher scores in all domains of the PFDI-20 ($P < 0.01$) and KHQ ($P < 0.05$), except for general health perception ($P = 0.34$) and bladder symptoms ($P = 1.0$) (Table 4). Women with POI and FI presented with a lower duration of gonadal failure ($P < 0.01$), and women with POI and POP did not show any association (data not shown).

Factors associated with UI, POP, and FI within women with POI

Table 5 presents the univariate and multivariate analysis for UI. For UI, we found during univariate analysis that not using HT ($P < 0.01$), higher weight ($P < 0.01$), higher BMI ($P < 0.01$), having completed basic education level ($P = 0.04$), standing position during work ($P = 0.03$), obesity ($P < 0.01$), higher mean age at POI diagnosis ($P < 0.01$), pregnancy ($P < 0.01$), vaginal ($P = 0.02$) and cesarean deliveries ($P = 0.04$), older age at menarche ($P = 0.01$), and abnormal karyotype ($P = 0.04$) were risk factors for UI, whereas sitting position during work was a protective factor for UI ($P < 0.01$). Multivariate analysis found that higher weight (odds ratio [OR] 1.047 [1.018-1.076], $P < 0.01$) and previous pregnancy (OR 1.627 [1.169-2.266], $P < 0.01$) were risk factors for UI.

Fecal incontinence presented the following associated variables at univariate analysis: having a postgraduate degree ($P = 0.04$), gravidity ($P = 0.04$), and shorter menopause duration ($P = 0.03$). For POP, univariate analysis found that higher

TABLE 1. *Baseline variables between POI and control groups*

Variables	POI (n = 150)	Control (n = 150)	Total	P^a
Age, y				
<20	6 (9)	5.33 (8)	17	0.18
20-39	20 (30)	30.67 (46)	76	
30-39	37.33 (56)	34.67 (52)	108	
40-48	36.67 (55)	29.33 (44)	99	
Education level, y				
<8	14 (21)	23.49 (35)	56	0.01[a]
9-11	66.67 (100)	46.98 (70)	170	
11-15	12.67 (19)	20.13 (30)	49	
>15	6.67 (10)	9.40 (14)	24	
Race				
White	52 (78)	49.33 (74)	152	0.42
Black	10.67 (16)	14 (21)	37	
Asian	2 (3)	5.33 (8)	11	
Hispanic non-white	32.67 (49)	30 (45)	94	
Other	2.67 (4)	1.33 (2)	6	
Tobacco use				
Yes	6 (9)	8.67 (13)	22	0.37
No	94 (141)	91.33 (137)	278	
Gravidity				
0	67.33 (101)	24.67 (37)	138	<0.01[a]
1	14 (21)	30.36 (34)	65	
≥2	18.67 (28)	50.00 (56)	97	
Presence of comorbidities				
Yes	61.33 (92)	40 (60)	152	<0.01[a]
No	38.67 (58)	60 (90)	148	
Any endocrinopathies				
Yes	13.33 (20)	1.33 (2)	22	<0.01[a]
No	86.67 (130)	98.67 (148)	278	
Obesity				
Yes	18 (27)	26 (39)	66	0.09
No	82 (123)	74 (111)	234	
Diabetes				
Yes	5.33 (8)	2.67 (4)	12	0.23
No	94.67 (142)	97.33 (146)	288	
Other comorbidities				
Yes	45.33 (68)	18.67 (28)	96	<0.01[a]
No	54.67 (82)	81.33 (122)	204	
Urinary incontinence				
Yes	27.33 (41)	37.33 (56)	97	0.06
No	72.67 (109)	62.67 (94)	202	
Does UI impair your QoL				
Yes	12 (18)	21.33 (32)	50	0.03[a]
No	88 (132)	78.67 (118)	250	
Fecal incontinence				
Yes	8 (12)	4 (6)	18	0.14
No	92 (138)	96 (144)	282	
Prolapse symptoms				
Yes	9.33 (14)	8 (12)	26	0.68
No	90.67 (136)	92 (138)	274	
Standing position during work				
Yes	68.67 (103)	64.67 (97)	200	0.46
No	31.33 (47)	35.33 (53)	100	
Sitting position during work				
Yes	52 (78)	48 (72)	150	0.48
No	48 (72)	52 (78)	150	
Carry weight during activities				
Yes	18 (27)	14 (21)	48	0.34
No	82 (123)	86 (129)	252	

POI, premature ovarian insufficiency, QoL, quality of life; UI, urinary incontinence.
[a]Chi-square test; values in % and n into parenthesis.

weight ($P < 0.01$), higher BMI ($P < 0.01$), having completed high school ($P = 0.03$) and elementary school ($P = 0.24$), presence of comorbidities ($P < 0.01$), vaginal delivery ($P = 0.02$), and smaller mean thelarche ($P = 0.03$) were risk factors. Only higher weight (OR 1.046 [1.010-1.084], $P = 0.01$) and the presence of comorbidities (OR 8.75 [1.07-71.44], $P < 0.01$) remained associated with POP during the multivariate analysis. No variables were associated with FI during the multivariate analysis (data not shown).

DISCUSSION

Although hypoestrogenism is related to genitourinary symptoms, and this might have possible implications for the etiopathogenesis of pelvic floor dysfunction,[17] our study

TABLE 2. *Comparison between the Oxford Modified Scale (PERF), and the PFDI-20 and KHQ questionnaire versus two groups (POI and control)*

Variables	POI			Control			P^a
	n	Mean	SD	n	Mean	SD	
P	70	2.29	0.89	88	2.17	0.81	0.46
E	70	4.49	3.76	88	4.14	3.15	0.91
R	70	2.24	1.93	88	2.11	1.66	0.88
F	70	4.20	3.10	88	4.91	3.69	0.19
PFDI-20							
POPDI6	150	5.03	9.46	150	7.25	10.87	0.01
CRAD8	150	9.35	13.32	150	9	12.40	0.83
UDI6	150	11.94	20.04	150	13.08	30.14	0.34
Total	150	26.33	37.21	150	29.33	35.41	0.09
KHQ							
General health perception	150	35.33	20.72	150	30.50	21.84	0.06
Bladder problem impact	150	7.33	17.64	150	13.56	26.78	0.08
Daily activities limitation	150	5.11	14.95	150	7.56	19.17	0.51
Physical limitation	150	6.78	17.81	150	9.89	20.90	0.08
Social limitation	150	3.07	11.91	150	3.48	11.16	0.81
Personal limitation	150	4.01	14.96	150	4.13	14.67	0.81
Emotions	150	5.63	20.75	150	6.37	18.54	0.04
Sleep	150	7.44	17.86	150	6.67	18.32	0.30
Severity	150	10.67	18.25	150	13.89	21.54	0.36
Frequency	150	0.89	1.09	150	0.81	1.03	0.52
Nocturia	150	0.93	0.95	150	0.81	0.90	0.23
Urgency	150	0.39	0.79	150	0.41	0.75	0.47
Overactive bladder	150	0.30	0.66	150	0.34	0.72	0.66
Stress urinary incontinence	150	0.27	0.65	150	0.41	0.83	0.09
Nocturnal enuresis	150	0.04	0.30	150	0.01	0.12	0.64
Coital incontinence	150	0.09	0.40	150	0.06	0.29	0.77
Infections	150	0.25	0.68	150	0.33	0.74	0.20
Bladder pain	150	0.21	0.56	150	0.25	0.61	0.53
Others	150	0	0	150	0.05	0.33	0.08

KHQ, King's Health Questionnaire; PERF, P—power; E—endurance; R—repetitions; F—fast; PFDI-20, Pelvic Floor Distress Inventory—20; POI, premature ovarian insufficiency.
[a]Mann-Whitney test.

did not find any significant difference in PFD between control and women with POI. On the contrary, we observed higher prolapse symptoms in women from the control group, according to PFDI-20. This might be due to the control group who presented with a higher mean number of pregnancies ($P < 0.01$), vaginal deliveries ($P < 0.01$), and cesarean sections ($P < 0.01$), and these variables are already associated with POP according to previous literature.[18]

Regarding the KHQ—an instrument that is useful for assessing the severity of UI and other urinary symptoms—we also did not find a significant difference in almost all domains between the groups except for more anxiety, nervousness, and depression in the control group; furthermore, the latter presented a higher impact on women's quality of life when investigating UI. UI may be present in women with POP[19] and also reduce quality of life, as it can be related with depression and anxiety.[20]

When analyzing women with POI who presented with UI, a higher score for POP, UI, and FI was found by the PFDI-20 questionnaire ($P < 0.05$), and also most of the domains of the KHQ, except for general health perception and bother with bladder issues ($P < 0.05$). Most of the participants did not use HT and had a later diagnosis, probably indicating a larger hypoestrogenic period on structures that would support continence. This association was not found in women with POI with FI and POP; women with POI and FI presented a shorter gonadal failure duration. Tan et al[21] did not find an association between amenorrhea duration and HT use versus UI incidence in women with POI; however, their study reported a shorter gonadal failure duration.

There was no difference between the UI prevalence between POI and control women, and these data are similar to that from the study by Tan et al,[21] who did not find significant differences between the groups; however, women

TABLE 3. *Modified Oxford Scale results between the groups (POI and control)*

Groups	Modified Oxford Scale (n [%])						P^a
	1	2	3	4	5	Total	
POI	13 (18.57)	30 (42.86)	22 (31.43)	4 (5.71)	1 (1.43)	70	
Control	18 (20.45)	41 (46.59)	25 (28.41)	4 (4.55)	0	88	0.87
Total	31	71	47	8	1	158	

POI, premature ovarian insufficiency.
[a]Chi-saquare test.

TABLE 4. *Data regarding clinical diagnosis, hormonal values, and PFDI-20 and KHQ scores from women with POI with and without UI*

	IU			wIU		
Variables	n	Mean	SD	n	Mean	SD
Duration of gonadal failure	33	126.48	116.50	62	111.87	89.14
Age at diagnosis	41	28.78[a]	8.62	109	24.31	8.56
Duration of diagnosis	41	8.89	8.96	109	10.48	8.34
Total duration using HT	35	106.43	104.80	102	118.82	104.04
PFDI-20						
POPDI6	41	10.98[a]	13.43	109	2.79	6.19
CRAD8	41	16.31[a]	18.03	109	6.74	9.96
UDI6	41	33.64[a]	26.52	109	3.78	6.89
Total score	41	60.92	49.07	109	13.31	19.83
KHQ						
General health perception	41	37.80	23.80	109	34.40	19.48
Bladder problem impact	41	22.76[a]	26.29	109	1.53	7.01
Daily activities limitation	41	15.85[a]	24.42	109	1.07	5.21
Physical limitation	41	17.48[a]	27.37	109	2.75	10.02
Social limitation	41	9.49[a]	20.91	109	0.66	3.52
Personal limitation	41	10.00[a]	23.98	109	0.97	4.85
Emotions	41	15.72[a]	34.69	109	1.83	9.74
Sleep	41	15.45[a]	25.38	109	4.43	12.96
Severity	41	28.05[a]	25.74	109	4.13	7.49
Frequency	41	1.49[a]	1.19	109	0.67	0.96
Nocturia	41	1.32[a]	1.01	109	0.79	0.88
Urgency	41	0.78[a]	1.04	109	0.24	0.62
Overactive bladder	41	0.90[a]	0.92	109	0.07	0.33
Stress urinary incontinence	41	1.00[a]	0.92	109	0.00	0.00
Nocturnal enuresis	41	0.15[a]	0.57	109	0.00	0.00
Coital incontinence	41	0.32[a]	0.72	109	0.00	0.00
Infections	41	0.46[a]	0.87	109	0.17	0.57
Bladder pain	41	0.44[a]	0.81	109	0.12	0.40
Others	41	0.00	0.00	109	0.00	0.00

Mann-Whitney test.
CRADI8, Colorectal Anal Distress Inventory 8; HT, hormone therapy; KHQ, King's Health Questionnaire; PFDI-20, Pelvic Floor Distress Inventory—20; POI, premature ovarian insufficiency; POPDI6, Pelvic Organ Prolapse Distress Inventory 6; UDI 6, Urinary Distress Inventory 6; UI, urinary incontinence; wIU, without urinary incontinence.
[a]$P < 0.05$.

with POI presented a higher prevalence than the control group (20.1% vs 16.2%; $P =$ NS). Their control group was made of nulliparous women, and this could have influenced the lower rate of UI.

The prevalence of FI and POP was not statistically significant between the POI and control groups (8% vs 4%, and 9.33% vs 8%, respectively). To date, this study is the only one that analyzed these variables in women with POI. The analysis of this dysfunction in normoestrogenic adolescents and young adults has already been described in a previous study,[22] where they assessed the prevalence of PFD in women who were 19 to 24/25 to 30 years old, and found that FI prevalence was 1.8% in adolescents and 0.2% in younger women. For POP symptoms, the prevalence was 0.2% and 0.5%, respectively, for adolescents and younger women. Our rates were higher when compared with this study because despite being young adults, our mean age was higher than 30 years, which possibly explains the rate of FI and POP. However, it is important to remember that the sampling size calculation was not directed towards these two variables.

Pelvic floor muscle assessment was performed by the PERFECT scale. It does not have enough accuracy to establish an association between pelvic floor muscles (PFM) and PFD due to its subjectiveness and lower sensitivity[23]; however, digital palpation has been frequently used in the clinical scenario. Several authors have correlated digital palpation with objective methods,[24-26] and the International Continence Society presents digital palpation as a way of assessing PFM.[11]

Regarding the functional pelvic muscle floor assessment by the PERFECT scale, the POI and control groups did not present any meaningful difference. A higher grade 2 prevalence was seen for women with POI and control women (42.86% vs 46.58%). To date, there are no studies that have analyzed the correlation between pelvic floor muscle strength and presence of PFD within this population.

When we analyzed the POI group regarding the use of HT, we noted a trend for higher muscle power in women using HT when compared with nonusers, but with no statistically significant difference ($P = 0.11$). Despite women with POI using HT presented with higher muscle strength compared with women with POI not using HT; however, we cannot attribute that this is due to HT. On the contrary, since estrogen receptors exist in the vagina, bladder, urethra, and pelvic floor muscles,[4,7] we cannot say with certainty the opposite, either. Some studies have shown positive effects of estrogen on stress urinary incontinence (SUI), causing an increase in urethral closure pressure, improvement of transmission from abdominal pressure to proximal urethra, and increase in the functional capacity along the urethral length. This is probably due to an

TABLE 5. *Univariate and multivariate logistic regression for self-reported urinary incontinence (UI) in women with POI*

Variables		*P*	cOR[a] (95% CI%)	aOR[b] (95% CI)	*P*
Group	POI with HT (ref.)	—	1.00 (—)		
	POI without HT	0.03	2.42 (1.09-5.35)		
Age	(y)	0.05	1.046 (0.999-1.095)		
Weight	(kg)	<0.01	1.049 (1.022-1.76)	1.047 (1.018-1.076)	<0.01
Height	(m)	0.35	5.924 (0.141-248.756)		
Body mass index	(kg/m^2)	<0.01	1.124 (1.048-1.207)		
Education level	12 y or +	—	1.00 (—)		
	8-12 y	0.18	1.97 (0.73-5.29)		
	<8 y	0.04	3.46 (1.02-1.015)		
Education level	(y)	0.08	0.898 (0.794 – 1.015)		
Race	White (ref.)	—	1.00 (—)		
	Non-white	0.80	0.91 (0.44-1.87)		
Tobacco use	No (ref.)	—	1.00 (—)		
	Yes	0.68	1.36 (0.32-5.69)		
Standing position during work	No (ref.)	—	1.00 (—)		
	Yes	0.03	2.82 (1.14-6.94)		
Sitting position during work	No (ref.)	—	1.00 (—)		
	Yes	<0.01	0.37 (0.17-0.77)		
Carry weight during work	No (ref.)	—	1.00 (—)		
	Yes	0.09	2.13 (0.89-5.09)		
Comorbitidies	No (ref.)	—	1.00 (—)		
	Yes	0.07	2.07 (0.94-4.55)		
Diabetes	No (ref.)	—	1.00 (—)		
	Yes	0.51	1.64 (0.37-7.21)		
Obesity	No (ref.)	—	1.00 (—)		
	Yes	<0.01	3.15 (1.33-7.48)		
Endocrine diseases	No (ref.)	—	1.00 (—)		
	Yes	0.43	0.63 (0.20-2.01)		
Other diseases	No (ref.)	—	1.00 (—)		
	Yes	0.37	1.39 (0.67-2.85)		
Menstrual patterns	Never (ref.)	—	1.00 (—)		
	Menopause <40 y	0.01	3.01 (1.27-7.12)		
Menopause duration	(mos)	0.49	1.001 (0.997-1.006)		
Age of POI diagnosis	(y)	<0.01	1.062 (1.017-1.109)		
Duration of POI diagnosis	(y)	0.31	0.977 (0.935-1.021)		
Gravidity		<0.01	1.666 (1.213-2.288)	1.627 (1.169-2.266)	<0.01
Vaginal delivery		0.02	1.856 (1.092-3.157)		
Cesarean delivery		0.04	1.739 (1.009-2.996)		
Menarche	(y)	0.01	0.850 (0.752-0.962)		
Thelarche	(y)	0.08	0.912 (0.824-1.010)		
Pubarche	(y)	0.19	0.922 (0.815-1.042)		
Type of amenorrhea	Primary	—	1.00 (—)		
	Secondary	0.01	3.01 (1.27-7.12)		
Sexual activity	No (ref.)	—	1.00 (—)		
	Yes	0.13	2.02 (0.81-5.03)		
Physical activity with pelvic impact	No (ref.)	—	1.00 (—)		
	Yes	0.16	0.40 (0.11-1.44)		
Karyotype analysis	Normal (ref.)	—	1.00 (—)		
	Abnormal	0.04	4.40 (1.30-14.96)		
Use of HT	No (ref.)	—	1.00 (—)		
	Yes	<0.01	2.09 (1.23-3.54)		
HT type	Standard dosage (ref.)	—	1.00 (—)		
	High dosage	0.81	1.12 (0.44-2.85)		
	COC	0.14	0.29 (0.06-1.51)		
	Tibolone	0.96	1.04 (0.23-4.81)		
Duration for using HT	(mos)	0.56	0.998 (0.990-1.005)		
Total duration for using HT	(mos)	0.54	0.999 (0.995-1.003)		

95% CI, 95% confidence interval; COC, combined oral contraceptive; HT, hormone therapy; Ref.: reference.
[a]cOR (odds ratio) (n = 109 without UI and n = 41 with UI).
[b]aOR (odds ratio) = adjusted odds ratio (n = 101 without UI and n = 40 with UI).

increase in urethral closure at its lumen, because estrogen increases the thickness of the urethral wall.[27,28] In a recent study, which compared postmenopausal women with and without pelvic floor dysfunction, they observed a predominance of grade 2 muscle strength (39.7%), with no statistically significant difference among the groups.[24] Both studies suggest that women with hormonal abnormalities, especially estrogen deficiency, may develop weaker pelvic muscles. Apparently, the use of HT does not influence the concentration of intramuscular estrogen in postmenopausal women, suggesting that steroidogenesis may be more related to a genetic condition. Furthermore, this study detected that

steroid hormones are strongly associated with muscle potency and strength, and that resistance exercise may be a regulator of intramuscular steroidogenesis.[29] Therefore, perhaps perineal muscle strengthening exercises may be associated with improved quality of this muscle group in the POI population, possibly by recovering the steroid hormone effect. On the contrary, our study suggests that oral HT could be related to continence since a higher percentage of HT nonusers with UI was seen versus HT users ($P = 0.03$); however, this is a cross-sectional study, and for obvious reasons, we cannot infer causality and can attribute other possible factors in this analysis.

Higher weight and pregnancy were associated risk factors for UI. Our findings are similar to a previous study[30] that calculated the UI prevalence in younger participants and observed that 12% of women under 30 years reported UI. This group of women showed an association with urinary tract infection, nulliparity or primiparity, and higher weight. Hagglund et al[30] found that 23% of women under 30 years presented with UI while being nulliparous. A meta-analysis of prospective studies to assess the association between UI and obesity in young/middle-aged women has found a higher risk (68%) for UI in young/middle-aged women with excess weight. Tan et al[21] found that higher age, parity, and vaginal delivery were risk factors for SUI.

Women with increased weight and no comorbidities were found to be at risk for the development of POP. Higher weight could be related to structural damage or neurological dysfunction due to stress on the pelvic floor, secondary to intra-abdominal pressure.[31] Kudish et al[32] observed that overweight and obesity were associated with POP progression, whereas weight loss was not associated with prolapse regression, suggesting that the alteration caused to the pelvic floor due to weight might be reversible. Isik et al[33] found that hypertension and diabetes were risk factors for the development of POP regardless of BMI and age. However, more studies are necessary to assess POP development linked to systemic diseases.

The strengths of this study are as follows: to our knowledge, this is the second study addressing women with POI; we have added a group of women with POI who were not treated with HT because they started attending our outpatient clinic. Furthermore, there was a physical assessment of the pelvic floor in women with symptoms; the use of validated pelvic floor questionnaires; and the exploration of pelvic disorders other than UI, such as POP and FI. Weaknesses can be also noted: recall bias because some participants had to remember a few variables related to POI (although, we used medical records in case of missing information); no possibility for inferring causality because this is a cross-sectional study; we did not perform a sample size calculation for POP or FI, disorders with a lower prevalence than UI, and this might introduce a higher chance of type 2 error. Some variables of the multivariate analysis from POP and FI may have been significant due to the lack of control for multiple comparisons. Our prevalence of UI was higher than the previous study within POI and control women, but the difference between the groups was not so large. This might increase the possibility of type 2 error in this analysis as well; thus, our data for many of the comparisons made should be interpreted cautiously. However, the contributions of our data on PFD in patients with POI is important for obtaining a deeper understanding of the connection between hormones and the pelvic floor.

CONCLUSIONS

In summary, our study has demonstrated that women with POI did not present with significant differences for PFD and perineal muscle contraction when compared with women of the same age, BMI, and with preserved gonadal function. Women in the control group presented with more POP symptoms, higher impact of UI on quality of life, and emotional conditions (anxiety, depression, and nervousness), suggesting that women with POI using HT have normal development of PFD and that the control group presented with greater influence of parity—a nonmatched variable between the groups. Moreover, women with POI without HT who have urine loss, present with more PFD and a higher impact of urinary symptoms on quality of life according to the questionnaire; this might be related to HT use and later age at the time of diagnosis, and therefore, later treatment. Further studies are needed within this population, with more stratification of confounding variables, preferably with a cohort study design, so that we may identify the association between hormonal levels and pelvic floor muscle behavior.

REFERENCES

1. Webber L, Davies M, Anderson R, et al. ESHRE Guideline: management of women with premature ovarian insufficiency. *Hum Reprod* 2016;31:926-937.
2. Gandhi J, Chen A, Dagur G, et al. Genitourinary syndrome of menopause: an overview of clinical manifestations, pathophysiology, etiology, evaluation, and management. *Am J Obstet Gynecol* 2016;215:704-711.
3. Calik-Ksepka A, Grymowicz M, Rudnicka E, et al. Signs and symptoms, evaluation, and management of genitourinary tract consequences of premature ovarian insufficiency. *Prz Menopauzalny* 2018;17:131-134.
4. Smith P, Heimer G, Norgren A, Ulmsten U. Steroid hormone receptors in pelvic muscles and ligaments in women. *Gynecol Obstet Invest* 1990;30:27-30.
5. Smith P. Estrogens and urogenital tract. Studies on steroid hormone receptors and a clinical study on a new estradiol-releasing vaginal ring. *Acta Obstet Gynecol Scand Suppl* 1993;157:1-26.
6. Soderberg MW, Johansson B, Masironi B, et al. Pelvic floor sex steroid hormone receptors, distribution and expression in pre- and posmenopausal stress urinary incontinent women. *Acta Obstet Gynecol Scand* 2007;86:1377-1384.
7. Dumoulin C, Pazzoto Cacciari L, Mercier J. Keeping the pelvic floor healthy. *Climacteric* 2019;22:257-262.
8. Souza CE, Bezerra LM, Pereira RW, Moura TK, Oliveira RJ. Comparative study of pelvic floor function in continent and incontinent postmenopausal women. *Braz J Physical Therapy* 2009;13:535-541.
9. Kim CM, Jeon MJ, Chung DJ, Kim SK, Kim JW, Bai SW. Risk factors for pelvic organ prolapse. *Int J Gynaecol Obstet* 2007;98:248-251.
10. Staller K, Townsend MK, Khalili H, et al. Menopausal hormone therapy is associated with increased risk of fecal incontinence in women after menopause. *Gastroenterology* 2017;152:1915-1921.
11. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Int Urogynecol J* 2010;21:5-26.
12. Associacion Medica Mundial. Declaración de Helsinki de la Asociación Médica Mundial. Principios éticos para las investigaciones medicas en

seres humanos; 2013. Available at: https://www.wma.net. Accessed September 12, 2019.
13. Munro MG, Critchley HOD, Broder MS, Fraser IS. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynecol Obstet* 2011; 113:3-13.
14. Arouca MA, Duarte TB, Lott DA, et al. Validation and cultural translation for Brazilian Portuguese version of the Pelvic Floor Impact Questionnaire (PFIQ-7) and Pelvic Floor Distress Inventory (PFDI-20). *Int Urogynecol J* 2016;27:1097-1106.
15. Tamanini JT, D'Ancona CA, Botega NJ, Rodrigues Netto N Jr. [Validation of the Portuguese version of the King's Health Questionnaire for urinary incontinent women]. *Rev Saude Publica* 2003;37:203-211.
16. SAS Institute. The SAS system for Windows. Release 9.2. Cary, NC; SAS Institute; 2011.
17. Erekson EA, Li FY, Martin DK, Fried TR. Vulvovaginal symptoms prevalence in postmenopausal women and relationship to other menopausal symptoms and pelvic floor disorders. *Menopause* 2016;23:368-375.
18. Horst W, do Valle JB, Silva JC, Gascho CLL. Pelvic organ prolapse: prevalence and risk factors in a Brazilian population. *Int Urogynecol J* 2017;28:1165-1170.
19. Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. *Lancet* 2007;369:1027-1038.
20. Miner PB Jr. Economic and personal impact of fecal and urinary incontinence. *Gastroenterology* 2004;126 (1 Suppl 1):S8-S13.
21. Tan R, Pu D, Cao J, et al. Prevalence of stress urinary incontinence in women with premature ovarian insufficiency. *J Womens Health (Larchmt)* 2018; doi: 10.1089/jwh.2018.6935 [Epub ahead of print].
22. Parden AM, Griffin RL, Hoover K, et al. Prevalence, awareness, and understanding of pelvic floor disorders in adolescent and young women. *Female Pelvic Med Reconstr Surg* 2016;22:346-354.
23. Borello-France DF, Handa VL, Brown MB, et al. Pelvic-floor muscle function in women with pelvic organ prolapse. *Phys Ther* 2007;87:399-407.
24. Frota IPR, Rocha ABO, Neto JAV, et al. Pelvic floor muscle function and quality of life in postmenopausal women with and without pelvic floor dysfunction. *Acta Obstet Gynecol Scand* 2018;97:552-559.
25. Volloyhaug I, Morkved S, Salvesen O, Salvesen KA. Assessment of pelvic floor muscle contraction with palpation, perineometry and transperineal ultrasound: a cross-sectional study. *Ultrasound Obstet Gynecol* 2016;47:768-773.
26. Albrich S, Steetskamp J, Knoechel SL, Porta S, Hoffmann G, Skala C. Assessment of pelvic floor muscle contractility: digital palpation versus 2D and 3D perineal ultrasound. *Arch Gynecol Obstet* 2016;293:839-843.
27. Sartori MG, Feldner PC, Jarmy-Di Bella ZI, et al. Sexual steroids in urogynecology. *Climacteric* 2011;14:5-14.
28. Al-Badr A, Ross S, Soroka D, Drutz HP. What is the available evidence for hormone replacement therapy in women with stress urinary incontinence? *J Obstet Gynaecol Can* 2003;25:567-574.
29. Pollanen E, Kangas R, Horttanainen M, et al. Intramuscular sex steroid hormones are associated with skeletal muscle strength and power in women with different hormonal status. *Aging Cell* 2015;14:236-248.
30. Hagglund D, Olsson H, Leppert J. Urinary incontinence: an unexpected large problem among young females. Results from a population-based study. *Fam Pract* 1999;16:506-509.
31. Greer WJ, Richter HE, Bartolucci AA, Burgio KL. Obesity and pelvic floor disorders: a systematic review. *Obstet Gynecol* 2008;112 (2 Pt 1): 341-349.
32. Kudish BI, Iglesia CB, Sokol RJ, et al. Effect of weight change on natural history of pelvic organ prolapse. *Obstet Gynecol* 2009;113:81-88.
33. Isik H, Aynioglu O, Sahbaz A, Selimoglu R, Timur H, Harma M. Are hypertension and diabetes mellitus risk factors for pelvic organ prolapse? *Eur J Obstet Gynecol Reprod Biol* 2016;197:59-62.

