Menopausal symptoms in average-age menopause and premature ovarian insufficiency

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Abstract

Objectives: There is limited data on the prevalence and severity of menopausal symptoms among the Canadian population. This study aims to characterize and compare the prevalence and severity of menopausal symptoms among Canadian women experiencing menopause around the average age and those with premature ovarian insufficiency.

Methods: This cross-sectional observational study included women attending specialized menopause and premature ovarian insufficiency clinics at an academic center in Toronto, Canada. Participants completed a standardized intake questionnaire and the Menopause Rating Scale, a validated instrument assessing psychological, somato-vegetative, and urogenital symptoms. Symptom prevalence and severity were compared between cohorts using nonparametric and categorical statistical tests.

Results: The study included 374 women experiencing menopause at an average age (median age 53 y) and 149 women with premature ovarian insufficiency (median age 34 y). Menopausal symptoms were common in both groups, with most women reporting symptoms in at least one domain. Urogenital symptoms were the most prevalent and severe across cohorts. Total Menopause Rating Scale scores were higher among women with menopause compared with premature ovarian insufficiency ($P = 0.003$), driven by greater somato-vegetative symptom burden ($P = 0.002$); psychological and urogenital symptom scores did not differ significantly between groups.

Conclusions: Menopausal symptoms are common and frequently severe for both average-age menopause and premature ovarian insufficiency. Younger age in premature ovarian insufficiency may not confer protection against psychological or urogenital symptoms, given similar symptom burden with average-age menopause. This underscores the need for proactive, comprehensive symptom assessment and management—particularly for urogenital and sexual health—in all individuals experiencing estrogen deficiency.

Key Words: Menopausal symptoms, Menopause Rating Scale, Menopause, Premature ovarian insufficiency, Urogenital symptoms.

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Women spend a considerable portion of their lives in the perimenopausal and postmenopausal state, during which progressive ovarian senescence and the resulting hypoestrogenic milieu exert widespread effects on physical, psychological, and sexual health.[1] In Canada, the average age of menopause is ~51 years; however, in cases of premature ovarian insufficiency (POI), this occurs before age 40, leading to an earlier onset of symptoms and other long-term health consequences.[2] Regardless of the cause—natural aging, POI, or iatrogenic loss of ovarian function—hypoestrogenism can manifest as a constellation of symptoms. These include vasomotor symptoms (hot flashes, night sweats), genitourinary symptoms (vaginal dryness or itching, dyspareunia, urinary frequency or urgency, recurrent urinary tract infections), musculoskeletal changes (arthralgias, myalgias), psychological and cognitive symptoms (mood changes, irritability, depression or anxiety, impaired concentration, memory lapses), dermatologic and hair changes (dry skin, thinning hair), and sexual dysfunction (decreased sexual desire, reduced arousal, difficulty achieving orgasm). These symptoms can be highly bothersome, and both women undergoing menopause at

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the average age and those with POI frequently report significant reductions in quality of life.[1,2]

There are also long-term health implications of estrogen deficiency. Estrogen plays a protective role in cardiovascular and bone health, and the menopause transition is associated with increased risks of cardiovascular disease and osteoporosis.[3] Women who enter menopause prematurely—either due to POI or surgically induced ovarian failure—face an even more prolonged period of hypoestrogenism and its sequelae.[2,3]

In Canada, ~10 million women aged 40 and greater are estimated to be in the perimenopausal, menopausal, or postmenopausal state. A study published by the Menopause Foundation of Canada found that over 95% of women between the ages of 40 and 60 experience at least one symptom associated with menopause.[4] There are no Canadian-specific estimates of POI in the literature, but the global prevalence of POI is considered as high as 3.7%.[5,6] Thus, not only do individual women spend many years in a hypoestrogenic state, but also a substantial proportion of the Canadian population is living with these experiences at any given time. Evidence from a 2005 US National Health and Wellness Survey found that symptomatic women aged 40-64 reported significantly poorer health-related quality of life than asymptomatic peers.[1] Similarly, a systematic review and meta-analysis by Li et al[7] demonstrated that women with POI have significantly lower health-related quality of life scores compared with age-matched healthy controls. However, few studies compare symptoms between Canadian women experiencing menopause at the average age and those with POI, despite important differences in age of onset and underlying etiology.[8] Studies often contrast these groups with age-matched reproductive-age controls.[5,7,8] Moreover, findings from the United States and European populations are often extrapolated to the Canadian context, particularly for POI, where Canadian-specific data remain limited.

This study aims to characterize and compare the prevalence of menopausal symptoms among Canadian women undergoing menopause at the average age and those with POI. POI is defined according to the European Society of Human Reproduction and Embryology (ESHRE) criteria as loss of ovarian function before age 40, characterized by oligo- or amenorrhea for at least 4 months and elevated gonadotropin levels.[8] Understanding the scope and nature of symptoms in both groups—and how they differ—is essential for clarifying the overall impact of declining ovarian function and for guiding future research into targeted, population-specific treatment strategies.[8]

METHODS

This cross-sectional observational study was conducted at two specialized clinics located in Toronto, Ontario: the Menopause Clinic and the Premature Ovarian Insufficiency Clinic. Patients were recruited from both clinics for participation in the study. These clinics assess women referred often by primary care providers or obstetricians-gynecologists for management of average-age menopause and POI. Referral criteria for the menopause clinic included perimenopausal and postmenopausal women over age 40 with validated menopausal symptoms, specifically related to menopause or abnormal uterine bleeding around the age of menopause. Referral criteria required for the POI clinic included age under 40, follicle-stimulating hormone levels > 25 IU/L on two occasions, oligomenorrhea or amenorrhea presenting over 3-4 months, presence or absence of menopausal symptoms, and negative pregnancy test. Participants were required to provide informed consent in English, independently or with a translator.

At their initial visit, participants completed a standardized questionnaire capturing demographic information, reproductive and gynecologic history, age of last menstrual period, menopausal symptom onset, prior menopause treatments, and relevant surgical history. Personal and family histories of major medical conditions—including cancers, bone disorders, and autoimmune diseases—were recorded, along with current and past treatments. Tobacco, alcohol, and recreational drug use histories were also obtained.

Menopausal symptoms were evaluated using the menopause rating scale (MRS), which is a self-administered, internationally validated questionnaire developed in the early 1990s to assess 11 symptoms that are grouped into three subdomains: four psychological (depressive mood, irritability, anxiety, physical and mental exhaustion), four somato-vegetative (hot flushes/sweating, heart discomfort, sleep problems, joint and muscular discomfort), and three urogenital (sexual problems, bladder problems, vaginal dryness) symptoms.[9] Each symptom is rated on a five-point ordinal scale from none to very severe symptoms (0-4). The total MRS score is calculated as a sum of all 11 items, and the validated severity cutoffs are as follows: none or very mild (0-4), mild (5-8), moderate (9-16), and severe (16+). The total score for the subdomains (psychological, somato-vegetative, urogenital) was also explored, but there are differences among studies on the specific cutoffs for level of severity. Generally, higher scores indicate more severe symptoms, and the scale used in this study is found in Appendix 1, Supplemental Digital Content 1, http://links.lww.com/MENO/B549. Although the MRS was originally developed for women in the perimenopause to postmenopause phases, it has been used for the POI population and captures domains relevant to estrogen deficiency regardless of age of onset.

Baseline clinical characteristics of women with POI and those with average-age menopause were summarized as medians with interquartile ranges for continuous variables and counts with percentages for categorical variables. Between-group differences were assessed using the Wilcoxon rank-sum test, χ^2 test, or Fisher exact test, as appropriate. All tests were two-sided with a significance threshold of 0.05. The statistical analysis was performed using statistical software R 4.2.1.

RESULTS

Baseline characteristics of participants

This study included 374 participants from the Menopause Clinic and 149 participants from the POI clinic, with

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median ages at the baseline visit of 53 years and 34 years, respectively. Age data were missing for 25 participants in the POI cohort (n = 124 with available data) and were complete for the menopause cohort. Median age at last menstrual period was 50 years among participants in the Menopause Clinic cohort (n = 78) and 33 years among participants in the POI cohort (n = 44). Analyses of age at last menstrual period were restricted to participants with available data after exclusion of missing values and non-applicable entries, including participants with POI who were still menstruating or had never experienced menses.

Within the POI cohort, menstrual status at baseline visit was available for 143 participants, with 54 reporting ongoing menstruation and 89 reporting amenorrhea; menstrual status was missing for 6 participants. Among those with amenorrhea, reported etiology included spontaneous (n = 35), iatrogenic (n = 43), and other causes (n = 10), with etiology unavailable for seven participants. Iatrogenic causes included ovarian insufficiency related to medication exposure, radiation therapy, chemotherapy, or surgically induced ovarian failure.

Baseline characteristics are presented in Table 1. Compared with participants with POI, women of average menopausal age reported higher rates of hypertension and alcohol use; however, the quantity of alcohol consumed was not assessed. Women with POI were more likely to report use of any hormone therapy. There were no between-group differences in prior diagnoses of mood or eating disorders. Missing data were assumed to be missing at random; no imputation was performed.

Prevalence and severity of menopausal symptoms

Menopausal symptoms were common in both cohorts, with only 12.3% of menopause participants and 14.7% of participants with POI reporting little to no symptoms. In the menopause cohort, the highest proportion of participants reporting symptoms was observed in the urogenital domain (84.5%), followed by the somato-vegetative (83.4%) and psychological (79.9%) domains. Overall, 51.3% in this group had a total MRS score in the severe range. Severe urogenital symptoms were reported by 53.5% of participants, compared with 44.4% for psychological symptoms and 28.1% for somato-vegetative symptoms.

Among women with POI, most reported urogenital symptoms (81.1%), followed by psychological (78.3%) and somato-vegetative (71.3%) symptoms. A total MRS score in the severe range was observed in 39.2% of participants with POI. Severe urogenital symptoms were reported by 43.4%, compared with 42% for psychological and 21% for somato-vegetative symptoms.

Comparison of menopausal symptoms in women with POI and average-age menopause

Total MRS scores were significantly higher ($P = 0.003$) among menopause participants compared with participants with POI. Menopause participants also reported significantly higher somato-vegetative symptom scores ($P = 0.002$). There were no significant between-group differences in psychological ($P = 0.950$) or urogenital ($P = 0.212$) symptom scores. Table 2 summarizes the comparison of menopausal symptoms between the cohorts.

As noted above, urogenital symptoms were the most reported in both groups. This category includes sexual problems (change in sexual desire, in sexual activity and satisfaction), bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence), dryness of vagina (sensation of dryness or burning in the vagina, difficulty with sexual intercourse). Among participants experiencing menopause at the average age, the highest proportion reported sexual problems (n = 262, 70.0%), followed by dryness of vagina (n = 240, 64.2%) and bladder problems (n = 203, 54.3%). A similar pattern was observed among those reporting severe or very severe symptoms, with sexual problems being most frequent (n = 122, 32.6%), followed by dryness of vagina (n = 94, 25.1%), and bladder problems (n = 42, 11.2%). Among participants with POI, sexual problems and vaginal dryness were equally the most reported symptoms

TABLE 1. Baseline characteristics for average-age menopause and premature ovarian insufficiency populations

Baseline characteristic	Overall (N = 523)	Menopause (n = 374)[a]	POI (n = 149)[a]	*P*
Age at baseline visit, median, (IQR)		53 [50-57]	34 [27-38]	< 0.001
Age of last menstrual period, median, (IQR)		50 [47-52]	33 [27-38]	< 0.001
Type 1 diabetes, n (%)	3 (1.5)	2 (3.1)	1 (0.7)	0.249
Stroke/mini-stroke, n (%)	8 (1.6)	4 (1.1)	4 (2.8)	0.236
Hypertension, n (%)	56 (11.1)	52 (14.5)	4 (2.8)	< 0.001
Anxiety disorder, n (%)	70 (14.0)	61 (17.1)	9 (6.2)	0.002
Depressive disorder, n (%)	30 (6.0)	22 (6.2)	8 (5.6)	0.959
Migraines, n (%)	60 (12.0)	24 (6.8)	36 (24.7)	< 0.001
Smoking, n (%)	58 (11.7)	39 (11.1)	19 (13.0)	0.662
Alcohol use, n (%)	271 (55.2)	206 (59.5)	65 (44.8)	0.004
Cannabis use (≤ 6 mo), n (%)	76 (15.3)	45 (12.7)	31 (21.4)	0.022
Anti-depressant use, n (%)	70 (13.8)	53 (14.2)	17 (12.7)	0.762
Benzodiazepine use, n (%)	27 (5.3)	25 (6.7)	2 (1.5)	0.023
Use of vitamins/herbals/natural medicines	226 (44.4)	143 (38.5)	83 (60.1)	< 0.001
Current use of hormonal therapy, n (%)	151 (29.2)	92 (24.7)	59 (40.7)	0.001

IQR, interquartile range; POI, premature ovarian insufficiency.
[a]Data are presented as median (IQR) or n (%). Sample sizes vary by characteristic due to missing data.

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TABLE 2. Comparison of Menopause Rating Scale scores for participants with average-age menopause and premature ovarian insufficiency

MRS domain	Severity category	Overall (N = 523)	Menopause (n = 374)	POI (n = 149)	P
Somatic	No/little	103 (19.9)	62 (16.6)	41 (28.7)	0.002
	Mild	72 (13.9)	46 (12.3)	26 (18.2)	
	Moderate	207 (40.0)	161 (43.0)	46 (32.2)	
	Severe	135 (26.1)	105 (28.1)	30 (21.0)	
Psychological	No/little	106 (20.5)	75 (20.1)	31 (21.7)	0.95
	Mild	65 (12.6)	46 (12.3)	19 (13.3)	
	Moderate	120 (23.2)	87 (23.3)	33 (23.1)	
	Severe	226 (43.7)	166 (44.4)	60 (42.0)	
Urogenital	No/little	85 (16.4)	58 (15.5)	27 (18.9)	0.212
	Mild	37 (7.2)	24 (6.4)	13 (9.1)	
	Moderate	133 (25.7)	92 (24.6)	41 (28.7)	
	Severe	262 (50.7)	200 (53.5)	62 (43.4)	
Total MRS score	No/little	67 (13.0)	46 (12.3)	21 (14.7)	0.003
	Mild	47 (9.1)	24 (6.4)	23 (16.1)	
	Moderate	155 (30.0)	112 (29.9)	43 (30.1)	
	Severe	248 (48.0)	192 (51.3)	56 (39.2)	

MRS, Menopause Rating Scale; POI, premature ovarian insufficiency.

(n = 87 for both, 58.4%), followed by bladder problems (n = 62, 41.6%). However, a greater proportion of participants with POI reported severe or very severe sexual problems (n = 31, 20.8%) compared with vaginal dryness (n = 21, 14.1%) and bladder problems (n = 17, 11.4%).

DISCUSSION

In this cross-sectional observational study of participants attending tertiary menopause and POI clinics, menopausal symptoms were highly prevalent and frequently severe in both groups. Urogenital symptoms represented the most reported symptom domain across cohorts, and sexual and vaginal dryness symptoms were both common and severe. Although participants experiencing menopause at the average age had higher overall symptom burden and greater somato-vegetative symptom severity, psychological and urogenital symptom scores did not differ significantly between the menopause cohort and participants with POI. This highlights the impact of estrogen deficiency on participants regardless of age of onset.

More than half of participants in the menopause cohort and nearly 40% of participants with POI reported severe overall symptoms as measured by the MRS. The symptom burden observed among participants experiencing menopause at the average age is higher than that reported in population-based studies.[10] This difference likely reflects the referral-based nature of specialized menopause clinics, where presumably women with worse symptoms are more likely to be referred for symptom management. In contrast, the literature lacks large population-based cohort studies evaluating the prevalence and severity of menopausal symptoms among women with POI, limiting the direct comparison with community-based samples. However, our findings are broadly consistent with a cross-sectional study of 293 Chinese women with POI by Huang et al[11], in which menopausal symptoms were reported by 70.6% of participants, compared with 85.3% in the present study. Huang et al[11] observed that 32.4% of participants reported moderate-to-severe symptoms, compared with 39.2% of participants in our cohort reported severe symptoms. Direct comparison between studies, specifically severity categories, is limited as Huang and colleagues used a different assessment instrument (Kupperman Menopausal Index). Both studies do show a clinically meaningful subset of women with POI experience significant symptom burden, even across diverse populations (Canadian vs. Chinese cohort). This reinforces the need for systematic symptom assessment in speciality menopause or POI care.

Across both cohorts, urogenital symptoms were the most prevalent and severe, with sexual problems and vaginal dryness reported most frequently, followed by bladder symptoms. These findings are consistent with prior literature demonstrating genitourinary symptoms are common and often undertreated.[12,13] Shea et al[13] assessed incidence of genitourinary syndrome of menopause in 529 participants in a specialized Canadian menopause clinic using the MRS. Their study found 74.4% reported vaginal dryness and 51% reporting moderate to very severe vaginal dryness, which is similar to our finding of 64.2% and 44.4%, respectively. Local hormonal therapies (eg, vaginal estrogen creams, vaginal hormone inserts) are considered the standard of care and yet, Shea et al[13] found only 10.9% of women before initial consultation were prescribed and using a local hormone therapy. In our study, only 24.7% of women with average-age menopause reported any current use of hormone therapy. This was more common in participants with POI at 40.7% ($P = 0.001$).

The prominence of sexual symptoms (change in sexual desire, in sexual activity or satisfaction) in both groups is also clinically significant, as these concerns are also frequently undertreated, despite their strong association with quality of life, relationship satisfaction, and psychological well-being.[14] Contributing factors may include social stigma or embarrassment with conversation avoidance with health care practi-

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tioners, misconceptions regarding the impact of menopausal symptoms on sexual function, and lack of awareness of treatment options among women and clinicians.[14] The close prevalence in both sexual problems and vaginal dryness captured for both cohorts may suggest their interlinked nature, as untreated sensation of dryness/burning in the vagina could affect an individual's desire or satisfaction in sexual activity.[15,16] Thus, management of genitourinary symptoms is central to addressing symptoms of vaginal dryness or dyspareunia. However, sexual problems in menopause or POI may persist despite adequate genitourinary symptom treatment as etiology is often multi-factorial.[13,15-17] Evidence-based treatment options for sexual dysfunction remain limited and symptom-specific, with few approved therapies targeting sexual desire or arousal, which continues to be a needed area of research. Currently, clinicians and women should be aware that management frequently often requires a multi-modal approach combining hormonal, non-hormonal, and psychosexual interventions.[15-17]

Women experiencing menopause at the average age had significantly higher total MRS scores and somato-vegetative symptom burden compared with those with POI. However, the absence of between-group differences in psychological and urogenital symptom scores suggests that the younger age inherent to the POI population may not mitigate the impact of estrogen deficiency on these domains. This finding is particularly relevant for women with POI, who may be experiencing menopausal symptoms with comparable severity to those of older women.

The strengths of this study include the use of a validated, internationally recognized symptom assessment tool and the inclusion of a relatively large cohort of women with POI, which is a population that remains underrepresented in menopause research. However, limitations include the referral-based study population, which may limit generalizability, and reliance on self-reported data. The cross-sectional assessment of symptoms at initial visit precludes evaluation of symptom progression over time, which is especially relevant for participants with POI with fluctuating ovarian function. Hormone therapy exposure was analyzed as a binary variable and did not account for formulation, dose, or duration. In addition, absence of specific estradiol or follicle-stimulating hormone measurements limited our ability to directly correlate hormonal status with symptom burden. Other potential confounders that were not captured include body mass index and ethnicity, both of which may be associated with variation in menopausal symptom prevalence and severity.[10]

CONCLUSIONS

In summary, this study demonstrates that menopausal symptoms are common and frequently severe among both average-age menopause participants and participants with POI in the Canadian context. Although overall symptom burden was higher among women experiencing menopause at the average age, psychological and urogenital symptoms were similarly prevalent across groups. These findings highlight the burden of menopausal symptoms in young patients with POI, and underscore the importance of proactive, comprehensive symptom screening in women. Collectively, these results emphasize the need for timely and effective management strategies for all individuals experiencing estrogen deficiency, with particular attention to urogenital and sexual health in both menopause and POI care.

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