Improving Menstrual Health throughout the Reproductive Life Course – Original Research Article

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Higher perceived stress during the COVID-19 pandemic increased menstrual dysregulation and menopause symptoms

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Abstract

Background: The increased stress the world experienced with the coronavirus disease (COVID-19) pandemic affected mental health, disproportionately affecting females. However, how perceived stress in the first year affected menstrual and menopausal symptoms has not yet been investigated.

Objectives: This study evaluates the effect that the first year of the COVID-19 pandemic had on female reproductive and mental health.

Methods: Residents in British Columbia, Canada, were surveyed online as part of the COVID-19 Rapid Evidence Study of a Provincial Population-Based Cohort for Gender and Sex. A subgroup of participants (n = 4171), who were assigned female sex at birth (age 25–69 years) and were surveyed within the first 6–12 months of the pandemic (August 2020–February 2021), prior to the widespread rollout of vaccines, was retrospectively asked if they noticed changes in their menstrual or menopausal symptoms, and completing validated measures of stress, depression and anxiety.

Design: This is a population-based online retrospective survey.

Results: We found that 27.8% reported menstrual cycle disturbances and 6.7% reported increased menopause symptoms. Those who scored higher on perceived stress, depression and anxiety scales were more likely to report reproductive cycle disturbances. Free-text responses revealed that reasons for disturbances were perceived to be related to the pandemic.

Conclusion: The COVID-19 pandemic has highlighted the need to research female-specific health issues, such as menstruation. Our data indicate that in the first year of the pandemic, almost one-third of the menstruating population reported disturbances in their cycle, which was related to percieved stress, depression and anxiety scores.

Keywords

anxiety, coronavirus disease 2019, depression, females, reproductive cycles, stress, women

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic led to closures of public places, strict health regulations and limited social interactions. These changes, along with the uncertainty of the pandemic, resulted in increased perceived levels of stress, depression and anxiety.[1,2] Women and gender-diverse individuals exhibited greater indices of distress, including heightened risk for mental health disorders than men throughout the COVID-19 pandemic.[1,3] Despite these findings, few studies have examined the potential effects of sex and gender in COVID-19 studies.[4–6] There has also been a lack of attention and research on the specific impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic on female health[7] which has contributed to alarming anecdotal reports of menstrual cycle irregularities following COVID-19 vaccination on social media.[8] These reported incidents, and resulting vaccine hesitancy due in part to fears of infertility,[9] underscored the importance of studying female cycles, which are now being closely examined in relation to COVID-19 vaccination.[6,10,11] However, there remains a need to examine the overall impact of the pandemic response on female menstrual cycles.

Menstrual cycle irregularities, perimenopause and menopausal disturbances can be important indicators of overall physical health.[12] Menstrual cycle irregularity is linked to metabolic dysfunction[13] and increased risk of cardiovascular disease.[14] Furthermore, vasomotor menopausal symptoms are related to white matter hyperintensities and cognitive disturbances.[15] Exposure to stress affects the hypothalamic–pituitary–gonadal (HPG) axes[16] as higher perceived stress is correlated with menopausal symptoms[17,18] and menstrual dysregulation.[19] Thus, it is not surprising that the COVID-19 pandemic and the associated increase in stress has led to the reports of disturbances to menstrual cycles.[20–23] Premenopausal people have reported irregularities in their menstrual cycles across different phases of the COVID-19 pandemic,[21] consistent with the literature indicating that heightened perceived stress is a predictor for menstrual irregularities.[24] Prolonged stress is also associated with an increased risk for psychiatric disorders,[25] and females reported higher depressive symptoms than males during the COVID-19 pandemic.[1,26] Moreover, studies show that depressed mood is associated with menstrual irregularities[27] meaning that pandemic-related stress may be affecting mental health and menstrual irregularities simultaneously or sequentially.

Given that stress and menstrual irregularities are connected,[24] and may play a role in mental health disturbances,[27] it is important to study these relationships. Heightened stress would likely have an impact on menstrual/menopausal irregularities, but to our knowledge, no study to date has examined these irregularities in relation to psychosocial outcomes. Here we examined whether perceived stress, anxiety or depression scores, and other factors that may play a role in perceived stress (age, number of children) within the context of the COVID-19 pandemic was related to reproductive cycles. We hypothesized that females would report an increase in the number of menstrual and menopausal symptoms during the first year of the pandemic and that these disturbances would be associated with stress, anxiety and depression levels.

Methods

Participant recruitment

The Rapid Evidence Study of a Provincial Population Based COhort for GeNder and SEx (RESPPONSE) was led by the Women's Health Research Institute in British Columbia (BC). All participants provided informed written consent prior to participation in RESPPONSE. Ethical approval was received from the BC Children's and Women's Research Ethics Board (H20-01421). Between mid-August 2020 and March 1, 2021, participants were recruited.[28] Survey responses were collected anonymously, with the exception of postal code. The survey took an average of 30 min to complete. All respondents who completed the survey were invited to enter a draw to win a US$100 e-gift card. The survey was open to residents of BC aged 25–69 years of all sexes and genders. A power analysis was conducted based on an expected 2% (± 1% 95% CI) seroprevalence of SARS-CoV-2 infection of individuals at the time of the survey in 2020–2021 for another study.[1] The targeted recruitment for each age strata (of mixed sex and gender) was 750. However, only participants who were assigned female sex at birth were eligible for this particular analysis (n = 5608). For analyses pertaining to menstrual changes, eligibility was restricted to female sex, not postmenopausal, not pregnant or within the first 6 months postpartum, and not on hormonal suppression drugs (n = 1866). In addition, we also conducted sensitivity analyses for menstrual changes to those people below 40 years of age to avoid conflation with possible symptoms of perimenopause (n = 810). For analyses of menopausal symptoms (e.g. hot flashes, changes in sleep quality, mood changes, brain fog and night sweats), eligibility was restricted to female sex and those who responded that they were postmenopausal (n = 2315), defined as the cessation of menstruation for 12 months. In addition, we also conducted sensitivity analyses for menopause status to those people above 50 years of age (n = 1978) to avoid conflation with possible symptoms of perimenopause, the period prior to menopause which starts after the onset of menstrual irregularity and ends after 1 year of after the final menstrual period. A flow diagram of recruitment, responses and inclusion among groups is given in Figure 1.

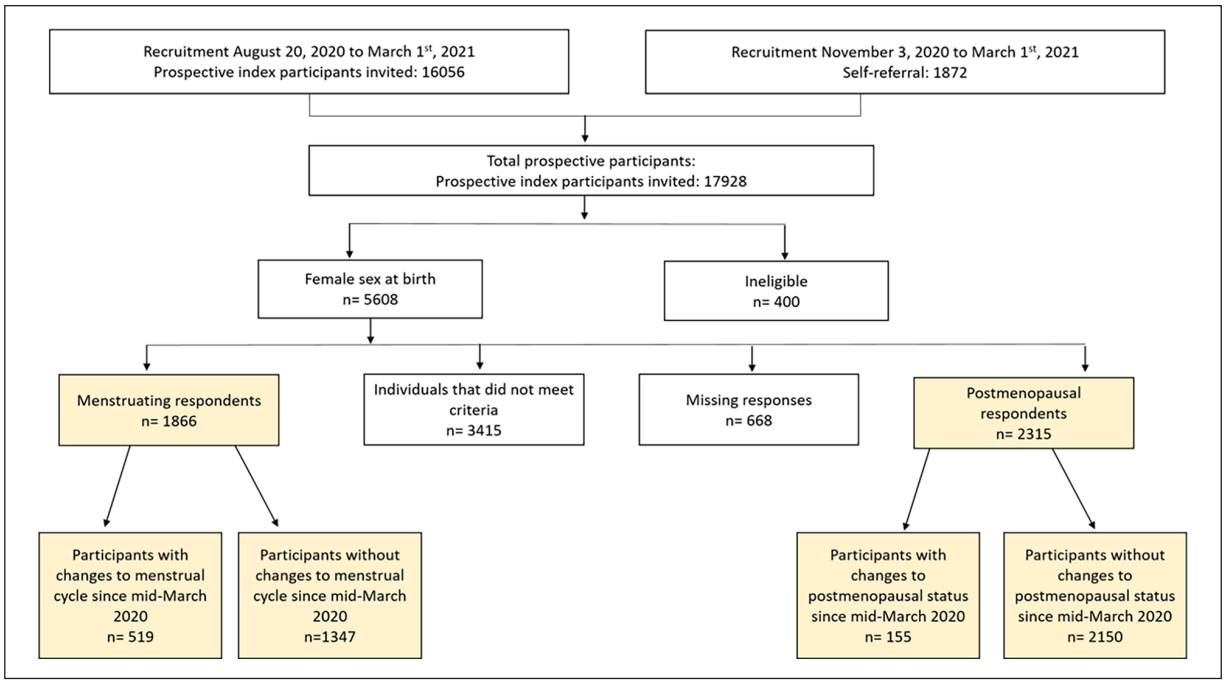

Figure 1. A flow diagram of prospective participants and respondents to the study.

Survey design and measures

The survey was tested for face validity, pilot-tested in June 2020 (n = 40) and implemented using Research Electronic Data Capture (REDCap).[29] The survey consisted of multiple modules, with the present analyses focused on female reproductive health questions surrounding menstrual cycle and menopause disturbances. All survey participants who were premenopausal were asked 'Since the COVID-19 pandemic and subsequent public health measures in mid-March 2020, have you noticed any changes to your menstrual cycle? (yes/no/not applicable due to hormonal suppression/not applicable other)', and participants who were postmenopausal were asked 'Have you noticed any changes to your postmenopausal status since mid-March 2020? (yes/no)'. Respondents who indicated changes to their menstrual cycle or postmenopausal status were prompted to check all that applied from a list of changes and provided with a free-text box (Survey questions for the reproductive characteristics are available in Supplementary Material section). All free-text responses were coded with a thematic analysis using the methods outlined in the study by Braun & Clarke (2006) to examine the potential variables influencing these changes.[30] Following this analysis, all responses were assigned to one of the two main themes: 'Non-pandemic-related' and 'Pandemic control measures'. 'Non-pandemic-related' comments were obvious changes to their health and reproductive system at the start of the pandemic or preceding the pandemic as mentioned in their responses. Alternatively, specific mentions of changes to their status or cycle, without medical reason, and stated as due to the pandemic were categorized as 'pandemic-related'. After separating all responses into these two themes, sub-themes were created to identify reproductive changes that occurred during the pandemic. Sub-themes were created if one or more respondents expressed the same theme in their free-text response. Validated scores of general pandemic stress, anxiety and depression were measured.[31,32] At the time of survey completion, participants were asked to recollect their mental health status during several pandemic phases that were based on the public health measures given at the time[1] (Phase 1 lasted from mid-March 2020 to mid-May 2020, Phase 2 lasted from mid-May 2020 to mid-June 2020, Phase 3 lasted from mid-June 2020 until the end of November 2020 and Phase 4 lasted from November 2020 to the date our survey closed; see Table 1 for a list of the public health measures during these phases).

General pandemic stress was measured using the CoRonavIruS Health Impact Survey (CRISIS) V0.3. This survey was developed and validated early in the COVID-19 pandemic to assess mental distress and resilience during the pandemic.[33] Participants were asked to self-report feelings of stress on a Likert-type scale from 1 (*not at all*) to 5 (*extremely*). Scores for this questionnaire range from 10 to 50 with higher scores indicating greater COVID-related stress.

Anxiety scores were calculated using the Generalized Anxiety Disorder questionnaire (GAD-7). The GAD-7 used self-reported feelings of anxiety on a Likert-type scale from 0 *(not at all*) to 3 (*nearly every day*) with scores ranging from 0 to 21. Scores above 10 suggest clinically

Table 1. Description of different COVID-19 time phases that were included in the survey.

COVID-19 phases	Public health control measures in BC
Phase 1 (mid-March 2020–mid-May 2020)	Closing of all businesses and a ban on gatherings, while essential services remain open. Essential services include, but are not limited to essential health services, transportation, food and agriculture service providers, liquor and cannabis stores, and vulnerable population service providers.
Phase 2 (mid-May 2020–mid-June 2020)	The start of reopening in BC, including hair salons, restaurants, libraries, office-based worksites, sports and childcare. Students K-12 returned to school on a gradual and part-time basis.
Phase 3 (mid-June 2020–August 2020)	A continued reopening including non-essential travel within the province, the reopening of the accommodation industry and movie theatres.
Phase 4 (September 2020–October 2020)	Restrictions tighten once again including a 10PM last call for liquor service, prohibition of events in banquet halls, and a cap on social gatherings
Phase 5 (November 2020–March 1, 2021)	Further restrictions placed on gatherings and services including a ban on gatherings at private residences for those outside of that household, mandatory masks in indoor and crowded settings, restrictions of sports facilities and gyms

significant levels of anxiety.[34] The Patient Health Questionnaire (PHQ-9) was used to measure self-reported symptoms of depression scores on a Likert-type scale from 0 (*not at all*) to 3 (*nearly every day*). Scores range from 0 to 27 with a score of 0–4 indicating minimal depression scores, 5–14 indicating mild-to-moderate depression scores and 15–27 indicating moderately severe to severe depression scores.[1] Internal consistency across data collection and Cronbach's alpha in the current sample was very good (CRISIS: $\alpha = 0.882$; GAD-7: 0.889, PHQ: $\alpha = 0.848$). The research team provided a list of local and provincial mental health resources following the completion of the psychosocial questions within the survey. In addition, the research team suggested that participants suspected of suffering setbacks in their mental or physical health by participating in the survey should speak to their doctor or mental health professional.

Statistical analyses

Analyses were carried out using R v.4.1.3.[35] The dataset was divided into two separate groups: people with menstrual periods and those in menopause (postmenopause) as described above, and summarized the percentages of those with any changes noted. We examined the relationship between mental health and changes in menopause status (any change versus no change) or menstruation (any change versus no change) by taking the average mental health scores across phases for each participant. These were entered in logistic regressions with change in menstruation or menopausal status as the outcome, and controlling for age, and presence of any coexisting chronic conditions (any of asthma, chronic obstructive pulmonary disease (COPD), chronic lung disease, insulin resistance, diabetes, hypertension, heart disease, coronary artery disease, heart failure, cardiac arrhythmia, stroke, deep vein thrombosis (DVT), peripheral vascular disease, liver disease/cirrhosis, kidney disease, autoimmune disorder, pneumonia or chronic neurologic or neuromuscular disorder). Significance was assessed using likelihood-ratio tests. Missing data were excluded from analyses on a per-variable basis. Participants missing data for any of the variables in the larger models would be excluded from that model, but included in models where they were not missing data. As the proportion of missing data was small for any given variable (Table 2), we did not choose to use imputation.

Results

Survey participants

Demographic information (age, ethnicity, gender, number of adults or children in the household, education, etc.) is seen in Tables 2 and 3. Of the premenopausal participants, 98.4% identified as women, 0.1% identified as men and 1.5% as gender diverse. Of the postmenopausal participants, 99% identified as women, 0.1% identified as men and 0.8% as gender diverse. Given that all of our participants were female sex, we have chosen to use the term females to refer to participants in our survey.

Changes in menstrual symptoms

Among our sample of premenopausal females, 519 (27.8% of the sample without suppressed cycles) reported that they had noticed changes in their menstrual cycle since March 2020. Of these 519 respondents, 44.3% indicated that their periods were more symptomatic (painful, more bleeding, etc.), 25.4%% indicated that their periods were longer, 23.7% said they were having fewer periods than before the pandemic, 21.8% noticed having more periods than normal, 15.7% said their periods had gotten shorter, 2.3% said their periods were less symptomatic. Options were not mutually exclusive and we received 784 answers from a potential 519 respondents. Moreover, 17.8% used free-text space to explain the changes to their menstrual cycles that they had noticed. The analysis of the free-text

Table 2. Demographic characteristics of respondents + denotes genderqueer, agender, two-spirit, other.

Menstruation changes					Postmenopausal changes			
Age (years)	Total	No	Yes	p	Total	No	Yes	p
	n = 1866	n = 1347	n = 519		n = 2305	n = 2150	n = 155	
25–29	183 (9.8%)	127 (9.4%)	56 (10.8%)	0.14	5 (0.2%)	4 (0.2%)	1 (0.6%)	<0.0001
30–39	627 (33.6%)	446 (33.1%)	181 (34.9%)		38 (1.6%)	34 (1.6%)	4 (2.6%)	
40–49	808 (43.3%)	602 (44.7%)	206 (39.7%)		174 (7.5%)	151 (7.0%)	23 (14.8%)	
50–59	242 (13.0%)	166 (12.3%)	76 (14.6%)		948 (41.1%)	854 (39.7%)	94 (60.6%)	
60–69	6 (0.3%)	6 (0.4%)	0 (0.0%)		1140 (49.5%)	1107 (51.5%)	33 (21.3%)	
Gender								
Woman	1837 (98.4%)	1333 (99.0%)	504 (97.1%)	0.006	2283 (99.0%)	2130 (99.1%)	153 (98.7%)	0.49
Man (female sex at birth)	1 (0.1%)	1 (0.1%)	0 (0.0%)		3 (0.1%)	3 (0.1%)	0 (0.0%)	
Non-binary, genderqueer, agender, two-spirit or other	28 (1.5%)	13 (1.0%)	15 (2.9%)		19 (0.8%)	17 (0.8%)	2 (1.3%)	
Indigenous								
Indigenous	72 (3.9%)	47 (3.5%)	25 (4.8%)	0.35	52 (2.3%)	47 (2.2%)	5 (3.2%)	0.047
Not indigenous	1706 (91.4%)	1235 (91.7%)	471 (90.8%)		2147 (93.1%)	2008 (93.4%)	139 (89.7%)	
Prefer not to answer	19 (1.0%)	15 (1.1%)	4 (0.8%)		13 (0.6%)	10 (0.5%)	3 (1.9%)	
Missing	69 (3.7%)	50 (3.7%)	19 (3.7%)		93 (4.0%)	85 (4.0%)	8 (5.2%)	
Latin American								
Latin American	40 (2.1%)	25 (1.9%)	15 (2.9%)	0.21	21 (0.9%)	18 (0.8%)	3 (1.9%)	0.16
Not	1819 (97.5%)	1316 (97.7%)	503 (96.9%)		2267 (98.4%)	2118 (98.5%)	149 (96.1%)	
Missing	7 (0.4%)	6 (0.4%)	1 (0.2%)		17 (0.7%)	14 (0.7%)	3 (1.9%)	
South Asian								
Not	1800 (96.5%)	1295 (96.1%)	505 (97.3%)	0.38	2258 (98.0%)	2112 (98.2%)	146 (94.2%)	0.012
South Asian	59 (3.2%)	46 (3.4%)	13 (2.5%)		30 (1.3%)	24 (1.1%)	6 (3.9%)	
Missing	7 (0.4%)	6 (0.4%)	1 (0.2%)		17 (0.7%)	14 (0.7%)	3 (1.9%)	
Black								
Black	19 (1.0%)	15 (1.1%)	4 (0.8%)	0.61	8 (0.3%)	8 (0.4%)	0 (0.0%)	1
Not Black	1840 (98.6%)	1326 (98.4%)	514 (99.0%)		2280 (98.9%)	2128 (99.0%)	152 (98.1%)	
Missing	7 (0.4%)	6 (0.4%)	1 (0.2%)		17 (0.7%)	14 (0.7%)	3 (1.9%)	

(Continued)

Table 2. (Continued)

Menstruation changes					Postmenopausal changes			
Age (years)	Total	No	Yes	p	Total	No	Yes	p
	n = 1866	n = 1347	n = 519		n = 2305	n = 2150	n = 155	
White								
Non-White	368 (19.7%)	281 (20.9%)	87 (16.8%)	0.044	245 (10.6%)	222 (10.3%)	23 (14.8%)	0.077
White	1491 (79.9%)	1060 (78.7%)	431 (83.0%)		2043 (88.6%)	1914 (89.0%)	129 (83.2%)	
Missing	7 (0.4%)	6 (0.4%)	1 (0.2%)		17 (0.7%)	14 (0.7%)	3 (1.9%)	
Education								
More than high school	1705 (91.4%)	1232 (91.5%)	473 (91.1%)	0.93	1924 (83.5%)	1788 (83.2%)	136 (87.7%)	0.18
High school or less	159 (8.5%)	114 (8.5%)	45 (8.7%)		377 (16.4%)	358 (16.7%)	19 (12.3%)	
Missing	2 (0.1%)	1 (0.1%)	1 (0.2%)		4 (0.2%)	4 (0.2%)	0 (0.0%)	
No. of adults in household								
One	388 (20.8%)	273 (20.3%)	115 (22.2%)	0.65	649 (28.2%)	601 (28.0%)	48 (31.0%)	0.51
Three or more	364 (19.5%)	263 (19.5%)	101 (19.5%)		526 (22.8%)	488 (22.7%)	38 (24.5%)	
Two	1113 (59.6%)	810 (60.1%)	303 (58.4%)		1121 (48.6%)	1052 (48.9%)	69 (44.5%)	
Missing	1 (0.1%)	1 (0.1%)	0 (0.0%)		9 (0.4%)	9 (0.4%)	0 (0.0%)	
No. of children in household < 5								
None	1514 (81.1%)	1079 (80.1%)	435 (83.8%)	0.095	2225 (96.5%)	2076 (96.6%)	149 (96.1%)	0.39
One	239 (12.8%)	185 (13.7%)	54 (10.4%)		23 (1.0%)	22 (1.0%)	1 (0.6%)	
Two or more	70 (3.8%)	54 (4.0%)	16 (3.1%)		14 (0.6%)	12 (0.6%)	2 (1.3%)	
Missing	43 (2.3%)	29 (2.2%)	14 (2.7%)		43 (1.9%)	40 (1.9%)	3 (1.9%)	
No. of children in household 5–17								
None	996 (53.4%)	698 (51.8%)	298 (57.4%)	0.02	1935 (83.9%)	1819 (84.6%)	116 (74.8%)	0.004
One	379 (20.3%)	271 (20.1%)	108 (20.8%)		201 (8.7%)	182 (8.5%)	19 (12.3%)	
Two or more	464 (24.9%)	357 (26.5%)	107 (20.6%)		121 (5.2%)	105 (4.9%)	16 (10.3%)	
Missing	27 (1.4%)	21 (1.6%)	6 (1.2%)		48 (2.1%)	44 (2.0%)	4 (2.6%)	
Chronic health conditions								
None	1026 (55.0%)	776 (57.6%)	250 (48.2%)	0.0003	998 (43.3%)	944 (43.9%)	54 (34.8%)	0.029
One or more	839 (45.0%)	570 (42.3%)	269 (51.8%)		1300 (56.4%)	1199 (55.8%)	101 (65.2%)	
Missing	1 (0.1%)	1 (0.1%)	0 (0.0%)		7 (0.3%)	7 (0.3%)	0 (0.0%)	
Crisis score Phase 1								
M (SD)	27.8 (±8.0)	26.6 (±7.7)	30.9 (±8.0)	<0.0001	24.9 (±7.6)	24.6 (±7.4)	28.9 (±8.8)	<0.0001
Missing	63 (3.4%)	51 (3.8%)	12 (2.3%)		86 (3.7%)	78 (3.6%)	8 (5.2%)	

SD: standard deviation.

Table 3. Sample sizes for CRISIS, GAD-7 and PHQ-9 measures for Phase 1.

Menstruation changes					Postmenopausal changes			
Age	Total	No	Yes	p	Total	No	Yes	p
Crisis score Phase 1								
M (SD)	27.8 (±8.0)	26.6 (±7.7)	30.9 (±8.0)	<0.0001	24.9 (±7.6)	24.6 (±7.4)	28.9 (±8.8)	<0.0001
Missing	63 (3.4%)	51 (3.8%)	12 (2.3%)		86 (3.7%)	78 (3.6%)	8 (5.2%)	
Anxiety GAD-7 Phase 1								
M (SD)	6.9 (±5.2)	6.2 (±4.9)	8.7 (±5.5)	<0.0001	5.0 (±4.7)	4.8 (±4.6)	7.4 (±5.5)	<0.0001
Missing	49 (2.6%)	40 (3.0%)	9 (1.7%)		106 (4.6%)	100 (4.7%)	6 (3.9%)	
Depression PHQ-9 Phase 1								
M (SD)	6.5 (±5.2)	5.7 (±4.7)	8.6 (±5.9)	<0.0001	5.0 (±4.5)	4.8 (±4.4)	7.8 (±5.7)	<0.0001
Missing	61 (3.3%)	51 (3.8%)	10 (1.9%)		144 (6.2%)	134 (6.2%)	10 (6.5%)	

SD: standard deviation; GAD: generalized anxiety disorder; PHQ: Patient Health Questionnaire.

Table 4. Summary of free-text responses for changes noticed in menstrual cycles.

Theme categories Total n = 92	Themes	Sub-themes	Participant response excerpts
Non-pandemic-related n = 29 (31.5)	Age-related n = 15 (51.7)	Entering perimenopause n = 15 (51.7)	'I'm perimenopausal'; 'perimenopausal, irregular, unpredictable'
	Changes to medication or contraceptives n = 6 (20.6)	Changes to birth control (patch, pill, IUD) n = 4 (13.7)	'Removed IUD so periods are balancing out'; 'Started period after going off of birth control'
		Medication, supplements n = 2 (6.8)	' – I have recently stopped taking all those supplements and have noticed that my cycle in general is longer'; 'Had a period when I had xxx, otherwise I haven't had a period in a while'.
	Changes to reproductive system n = 8 (27.5)	Got pregnant or intended to n = 4 (13.7)	'I got pregnant in xx'; 'Stopped due to positive pregnancy test'
		Hysterectomy n = 4 (13.7)	'Cycle starting to return after ablation'; 'Had hysterectomy done in xx'
Pandemic control measures n = 63 (68.4)	Cycle length/ volume changes n = 57 (90.4)	Varying cycle timing (start/end) n = 33 (52.3)	'Cycle is longer. Used to be 28 days. Now 31-32 days'; 'My cycle is normally 28 days on average; in March it was 35 days, April 26 day, moving back to 30 days then 29'.
		Changes in period length n = 14 (22.2)	'Irregular. Both long and short'; 'Periods have become more irregular, sometimes long, sometimes short with some spotting in between'
		Volume changes (more or less bleeding) n = 10 (15.80)	'they are more variable. . . shorter, sometimes very light, other quite heavy and with more severe cramps'; 'Short, long and light or heavy period. No idea what is happening sort of periods'
	Periods are more symptomatic n = 6 (9.5)	Mood symptoms n = 3 (4.7)	'More mood swings'; 'Weird timing and more moody'
		Painful n = 3 (4.7)	'Extreme cramping throughout month of April'; 'Worse migraines'

Sample sizes are given and percentages of total sample are given in parentheses. 'xx' is used to censor private participant information.

responses indicated that there were twice as many respondents who indicated their changes in symptoms were due to the *Pandemic control measures* (Table 4). As those aged > 40 years are more likely to be experiencing perimenopause, which could create menstrual disturbances independent of psychosocial stress, we undertook a sensitivity analysis of those who were less than 40 years old. Of this subset (n = 810), 29.2% (n = 237) reported changes in their menstrual cycle since the pandemic began. In addition, 52.7% indicated that their periods were more symptomatic (painful, more bleeding, etc.), 32.1% indicated that their periods had gotten longer, 13.1% said they were having fewer periods than normal, 20.7% noticed having more periods than normal, 19.0% said their periods had gotten

Table 5. Summary of free-text responses for changes noticed in postmenopausal status.

Theme categories Total n = 111	Themes	Sub-themes	Participant response excerpts
Non-pandemic-related n = 22 (19.8)	Surgery n = 10 (45.4)	Hysterectomy/ovarian cysts n = 10 (45.4)	'I haven't had periods in years because I had a hysterectomy due to severe endometriosis. I have recently been going through hot flashes that I'm assuming are menopause-related'; 'breast tenderness, mammography found cysts'
	Changes to medication n = 7 (31.8)	Hormone replacement therapy (HRT) changes n = 7 (31.8)	'My postmenopausal symptoms became more severe because of changes in HRT prescription'; 'I . . .tried a few replacement medications'.
	Pre-existing conditions n = 5 (22.7)	Endometriosis and cancer n = 5 (22.7)	'I had endometrial biopsy xx procedure'; 'Bleeding due to bladder cancer'
Pandemic control measures n = 89 (80.1)	Menopause symptoms have worsened n = 69 (77.5)	Hot flashes and insomnia n = 46 (51.6)	'Hot flashes- haven't had them in years'; 'More insomnia and hot flashes, and painful dry eyes which I didn't have before'.
		Mood symptoms n = 13 (14.6)	'Felt lonely and depressed and hopeless'; 'More emotional and stronger symptoms'
		Vaginal dryness and skin irritation n = 7 (7.8)	'Vaginal dryness, painful sex, sweats'; 'More skin irritation'
		Headaches/migraines n = 2 (2.2)	'Migraine headaches, hot flashes'; 'Headaches'
	Irregular changes to health n = 20 (22.4)	Bleeding/abdominal pain n = 9 (10.1)	'One episode of postmenopausal bleeding'; 'Abdominal pain and cramps in middle lower area'.
		Weight changes and hair loss n = 8 (8.9)	'Slower metabolism/weight gain in different areas of body'
		Memory loss n = 1 (1.1)	'Memory is getting bad. . .feeling for words often'; 'I have felt more symptoms such as brain fog and hot flashes which I assume are hormone related'.

Sample sizes are given and percentages of total sample are given in parentheses. 'xx' is used to censor private participant information. HRT: hormone replacement therapy.

shorter, 2.1% said their periods were less symptomatic and 19.8% used free-text space to explain the changes to their menstrual cycles that they had noticed. Options were not mutually exclusive and we received 378 answers from a potential 237 respondents.

Changes in menopausal symptoms

Among our sample of postmenopausal females (n = 2305), 155 (6.7%) reported that they noticed changes in their postmenopausal status since mid-March 2020. Of this subset (n = 155), 16.1% indicated that they started bleeding again and 12.3% indicated that they were experiencing 'more menstrual symptoms'. In addition, 72.9% used free-text space to explain the changes to their postmenopausal status. The analysis of the free-text responses revealed that there were four times as many respondents who indicated changes to postmenopausal status falling into the 'due to the pandemic control measures' category (Table 5). As those aged < 50 years are more likely to be experiencing perimenopause, which could create menopausal disturbances independent of psychosocial stress, a sensitivity analysis that restricted to those ≥ 50 (n = 1978) was conducted. Of this subset, there were 127 (6.4%) who reported that they had noticed changes in their postmenopausal status since before the pandemic. Of this subset (n = 127), 18.1% indicated that they started bleeding again and 7.9% indicated that they were experiencing 'more menstrual symptoms'. In addition, 71.7% of this subset used free-text space to explain the changes to their postmenopausal status that they had noticed. Analysis of these free-text responses revealed that 19.8% of reported changes were associated with the onset of the pandemic and 80.1% were not pandemic-related.

Higher pandemic stress, anxiety and depression symptoms were related to more disturbances in menstrual and menopausal symptoms

Across both groups, higher average scores on the psychosocial measures were associated with increased odds of disturbances in their cycles or changes to postmenopausal status. For premenopausal females, the odds ratio (OR) for pandemic crisis score was 1.06 (95% CI: 1.04–1.08) (see in Supplementary Material), suggesting that the odds of disturbance increased by 6% for every increase in one point along the crisis scale. Controlling for age and chronic conditions, the estimated marginal proportion

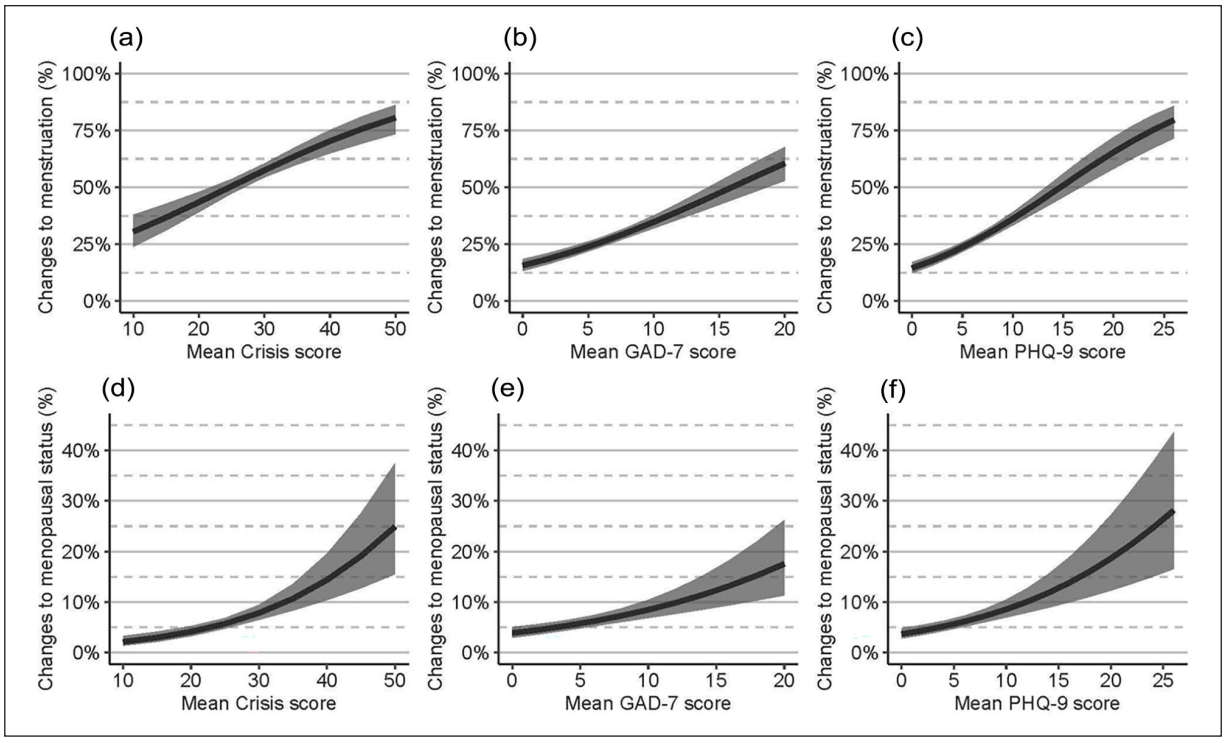

Figure 2. Changes to menstrual and menopausal status during early COVID-19 pandemic increased mean CRISIS scores, anxiety (GAD-7) and depression symptoms (PHQ-9) in females. Predicted marginal proportions and 95% CI from logistic regressions controlling for age and any comorbid chronic conditions. (a) CRISIS scores in females by changes to menstrual status. (b) GAD-7 scores in females by changes to menstrual status. (c) PHQ-9 scores in females by changes to menstrual status. (d) CRISIS scores in females by changes to menopausal status. (e) GAD-7 scores in females by changes to menopausal status. (f) PHQ-9 scores in females by changes to menopausal status. CI: confidence interval; GAD: generalized anxiety disorder; PHQ: Patient Health Questionnaire.

with disturbances when crisis score = 10 was 30.5% (95% CI: 24.0%–38.0%), and when crisis score = 40 was 70.3% (95% CI: 65.0%–75.2%) (Figure 2(a)). The OR for anxiety was 1.11 (95% CI: 1.08–1.14), suggesting that the odds of disturbance increased by 11% for every increase in one point along the GAD-7 scale. Controlling for age and chronic conditions, the estimated marginal proportion with disturbances when the GAD-7 score = 0 was 15.7% (95% CI: 13.2%–18.4%), and when the GAD-7 score = 10 was 34.8% (95% CI: 32.0%–37.6%) (Figure 2(b)). The OR for depression was 1.13 (95% CI: 1.10–1.15), suggesting that the odds of disturbance increased by 13% for every increase in one point along the PHQ-9 scale. Controlling for age and chronic conditions, the estimated marginal proportion with disturbances when the PHQ-9 score = 0 was 14.5% (95% CI: 12.3%–17.1%), and when the PHQ-9 score = 12 was 41.9% (95% CI: 38.2%–45.7%) (Figure 2(c)). Additional statistical outputs of the logistic regression can be found in the Supplementary Material.

For postmenopausal females, the OR for pandemic crisis score was 1.07 (95% CI: 1.04–1.10), suggesting that the odds of changes increased by 7% for every increase in one point along the crisis scale. Controlling for age and chronic conditions, the estimated marginal proportion with changes when crisis score = 10 was 2.1% (95% CI: 1.4%–3.3%), and when crisis score = 40 was 14.4% (95% CI: 10.4%–19.6%) (Figure 2(d)). The OR for anxiety was 1.09 (95% CI: 1.05–1.12), suggesting that the odds of changes increased by 9% for every increase in one point along the GAD-7 scale. Controlling for age and chronic conditions, the estimated marginal proportion with changes when the GAD-7 score = 0 was 3.9% (95% CI: 3.0%–5.1%), and when the GAD-7 score = 10 was 8.5% (95% CI: 6.9%–10.4%) (Figure 2(e)). The OR for depression was 1.09 (95% CI: 1.06–1.13), suggesting that the odds of changes increased by 9% for every increase in one point along the PHQ-9 scale. Controlling for age and chronic conditions, the estimated marginal proportion with changes when the PHQ-9 score = 0 was 3.7% (95% CI: 2.8%–4.8%), and when the PHQ-9 score = 12 was 10.1% (95% CI: 7.9%–12.7%) (Figure 2(f)). Additional statistical outputs of the logistic regression can be found in the Supplementary Material.

Relationship of menstrual or postmenopausal disturbances to number of children

As previous studies have found an association between the number of children and stress,[36] we also examined whether the number of children influenced our results.

We ran these analyses in premenstrual females who were below 40 years of age, choosing to exclude individuals who may have been perimenopausal based on age. There was no significant relationship between the number of children and whether or not the participant indicated they had disturbances to their menstrual cycle ($p = 0.100$). We next examined whether or not there was a relationship between menopausal disturbances and the number of children. There was a significant relationship ($p = 0.007$); however, when we used age as a covariate, the effect was no longer significant ($p = 0.409$). There were also no significant relationships between the number of children and pandemic stress scores, after controlling for age and changes to menstruation or menopause ($p = 0.167$ and 0.400, respectively).

Discussion

In a sample of 4171 surveyed females in BC that met our inclusion criteria, 27.8% of naturally cycling females had a disruption in their menstrual cycle and 6.7% of postmenopausal females indicated a change in their status, across the first year of the COVID-19 pandemic and prior to widespread rollout of COVID-19 vaccines. These disturbances to the reproductive cycles were related to higher scores of anxiety, depression and perceived stress, but not to the number of children, in both pre- and postmenopausal females. Females with higher stress scores were more likely to have experienced menstrual cycle phase disturbance with a doubling in the estimated proportion between crisis scores of 10 (31%) and 35 (64%) for premenopausal females and a doubling of postmenopausal changes between crisis scores of 10 (2%) and 20 (4%) for postmenopausal females. Similarly, higher scores on scales for anxiety and depression were associated with higher proportions of menstrual phase disturbance and postmenopausal changes (Figure 2(a)–(f)). We previously found that women had higher levels of perceived stress, depression and anxiety compared to men, using data from the same source.[1] Our findings here indicate that both pre- and postmenopausal females with higher levels of mental distress experienced greater disturbances in reproductive cycles. Stress has pervasive effects on mental and physical health, and our results add to the growing data that female-specific reproductive cycles are also affected.

During the first year of the pandemic, menstrual cycle disturbances were related to distress, anxiety and depression scores

We found that in the first year of the pandemic, 27.8% of the naturally cycling females surveyed had disturbances to their menstrual cycles. This is slightly lower than other surveys suggesting that 44% or more of females (including females who were younger than our own cohort 18–24 years of age) noticed changes in their cycles using fertility tracking devices.[37,38] Discrepancies between the percentages are likely due to the nature of our retrospective study as participants are relying on their memory as opposed to being able to track changes using fertility tracking devices. Other studies have suggested that the baseline rates of menstrual disturbances are ~15%.[39,40] Our findings are consistent with another study that showed an association between perceived stress during the COVID-19 pandemic and menstrual irregularities.[39] Although the literature suggests that parental responsibility increases perceived stress in women compared to men,[36] we found no evidence that there was a significant relationship between the number of children and changes in the menstrual cycle or in perceived stress in females younger than 40 years. Our data also indicate that higher anxiety scores and higher depression scores were associated with reported menstrual cycle disturbances.

Increased menopause symptoms were associated with increased perceived stress, anxiety and depression scores

We also found that fewer than 10% of postmenopausal females noticed changes to their menopausal status during the first year of the pandemic. Those who noticed changes in their status reported more menopausal symptoms, and furthermore, these individuals were more likely to score higher on scales examining perceived stress, depression and anxiety. Perimenopause is thought to be a time of heightened risk for mental health disruption[41] and those with menopausal symptoms may be at greater risk to develop psychiatric disorders.[42] The percentage of disturbances in reproductive symptoms was four times greater in our sample of premenopausal (27.8%) compared to postmenopausal females (6.7%). It is not clear why this large difference occurred but may be due to age, influence of stress on the HPG axis or level of stress overall. Indeed, other studies, including data from this same sample, have found that perceived stress, anxiety and depression scores were reduced with increasing age.[1,43] Thus, our findings of greater premenopausal versus postmenopausal disturbances align with data indicating mental health indices were lower for older adults during the first year of the pandemic.[1] Hypothalamic–pituitary–adrenal (HPA) axis activation, via stress, initially stimulates, and chronic activation inhibits the HPG resulting in menstrual abnormalities[44] and as these interactions vary across age,[44,45] this may also explain our findings as there would have been less HPA activation in the postmenopausal females in our sample. However, it is also possible that the premenopausal versus postmenopausal difference was due, in part, to the differences in the question posed to the two different groups, as our survey asked about menopause status rather than symptoms of menopause.

Relevance and limitations

Allostatic load, or the cumulative burden of a variety of stressors, affects cardiovascular and metabolic health.[46,47] However, it is important to acknowledge that female-specific factors, such as menstruation and menopause, are also impacted by chronic stress. Others have postulated that female health is cyclical as menstrual patterns correspond to changes in immune system function.[12] Moreover, there are specific interactions between gonadal hormones and immune cells[48] emphasizing important crosstalk.[49] It is possible that the mechanism behind stress and menstrual changes also involves glucocorticoid receptors in the endometrium.[50] Although SARS-CoV-2 infection and vaccines use can also disrupt reproductive cycles in the short term,[6,10] we do not believe this influenced our findings because we found that the seroprevalence of previous infection in this cohort was 2.9%[1] and vaccines were not widely available to the general BC population at the time of this survey. There are limitations to our study. This was a retrospective survey that required online access. However, our findings of high levels of menstrual disturbances are consistent with other studies using data from menstrual tracking apps.[37,38,51] Although one study using a menstrual cycle tracking app did find significantly more menstrual disturbances, these menstrual disturbances were not associated with stress.[38,51] However, that study did not use a validated measure of stress, nor did it explore the relationship with depressive or anxiety scores with menstrual disturbances.[51] In our survey, we did not obtain information on the normal levels of menstrual or menopausal symptoms pre-COVID-19 pandemic as we asked respondents to judge any changes themselves based on their pre-pandemic experience, and hence we are only able to cross study comparisons across scores for depression, anxiety and stress. This survey was limited to residents of the province of BC and our unique patterns of pandemic restriction measures may have impacted results (see Table 1). We also asked about menopausal status rather than menopausal symptoms and this may have reduced responses to this population of postmenopausal people. Future studies should query about different menopausal symptoms. Of course, menopausal status may be due to the passage of time, but this cannot be explained by our data as only individuals who had menopausal prior to the pandemic were included in that analyses. In our survey, we excluded individuals with pharmacologically suppressed cycles and did not query why people had suppressed cycles (e.g. which type of hormonal contraceptives, gender-affirming hormone therapy), which future studies could explore. In addition to the effects of the COVID-19 pandemic disproportionately affecting females, it is also well documented that the COVID-19 pandemic affected racial and sexual minorities to a higher degree.[52–54] There is also data suggesting that SARS-CoV-2 infection resulted in higher menopausal symptoms in Latin American women.[55,56] This is important to note as most of the participants in this study were predominantly cis-gendered, white women of higher education (more than high school). Future studies will focus on recruiting more diverse samples to obtain more generalizable results. We cannot rule out a selection bias in this study, as it is possible that individuals who experienced higher stress pre- and post-pandemic were more likely to participate. Similarly, those with menstrual abnormalities may be hyperaware of their menstrual cycle and led them to participate in the current study. In addition, it is also possible that participants with higher negative emotionality (as captured with higher depression/anxiety scores) are more likely to perceive changes in their cycles or symptoms.

Conclusion

The stress associated with the pandemic has impacted both our physical and mental health, and our findings suggest that this includes female-specific physical health characteristics. It is imperative to continue advancing the literature on external and internal factors impacting female reproductive health. Factors that can mitigate against the effects of stress, such as social support[57] and exercise[58] which were limited during the initial phases of the pandemic, may have exacerbated the negative outcomes on reproductive cycles for females. Given the lack of attention to women's health data,[59] more studies examining female-specific health indices are needed in the literature.

Declarations

Ethical approval and consent to participate

Ethical approval was received from the BC Children's and Women's Research Ethics board (H20–01421). All methods performed as a part of this study were in accordance with the UBC Research Ethics Board guidelines. Informed written consent to participate was obtained from participants.

Consent for publication

Written informed consent to publish was received in accordance with our institutional consent procedures.

Author contribution(s)

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Arianne Y. Albert: Conceptualization; Data curation; Formal analysis; Writing – review & editing.
Amy Booth: Investigation; Methodology; Project administration; Writing – review & editing.

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Anna Gottschlich: Conceptualization; Methodology; Writing – review & editing.
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Liisa A.M. Galea: Conceptualization; Project administration; Supervision; Writing – original draft; Writing – review & editing.

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Competing interests

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Availability of data and materials

Data cannot be shared publicly because of ethical restrictions. Data are available from the UBC Research Ethics Board (contact via cwreb@bcchr.ubc.ca) for researchers who meet the criteria for access to confidential data.

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Supplemental material

Supplemental material for this article is available online.

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