

## THE IMPACT OF PREVIOUS COVID-19 ON MENSTRUAL CYCLE REGULARITY AND WOMEN'S PSYCHOSOCIAL STATUS: QUALITY-OF-LIFE ASSESSMENT IN THE POST-COVID PERIOD

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### XULOSA

**Dolzarbliji.** Reproduktiv yoshdagи ayollarda post-COVID davrida hayz sikli buzilishlari va hayot sifatining pasayishi qayd etilgan, mavjud tadqiqotlar dizayni va ta'riflari turlicha.

**Maqsad.** Post-COVID hayz/ovarial disfunktisiyaning hayot sifati va stress bilan bog'liqligini baholash.

**Materiallar va usullar.** “ShifoNur” klinikasida ko'ndalang kesim tadqiqoti. n=144: post-COVID buzilishlar bilan (n=62), post-COVID buzilishlarsiz (n=52), nazorat — COVID-19 o'tkazmagan (n=30). Hayz ko'rsatkichlari FIGO mezonlari asosida, stress IES-R (10 band, 0–10; jami 0–100) orqali baholandi.

**Natijalar.** Tartibsiz hayz post-COVID buzilishlari bor guruhda 72,6% (45/62), nazoratda 30,0% (9/30; p<0,001); OR = 6,18 (95% IS 2,37–16,13). IES-R ballari mos ravishda  $88,24 \pm 2,9$ ,  $73,79 \pm 2,5$  va  $68,92 \pm 2,3$  (nazoratga nisbatan p<0,001 va p<0,01). “Yuqori stress” ulushi guruhlar orasida sezilarli farq qilmadi (p>0,05).

**Xulosa.** Post-COVID holat ayollarda hayz siklining tartibsizligi va yuqori stress yuklamasi bilan bog'liq, ayniqsa simptomlari borlarda. FIGO mezonlariga asoslangan hayz baholashi va qisqa IES-R skriningi post-COVID kuzatuv va maslahatni yaxshilashi mumkin.

**Kalit so'zlar:** COVID-19, hayz sikli, tartibsiz hayz kelishi, hayot sifati, IES-R, psixologik- ijtimoiy stress, ayollar salomatligi.

### РЕЗЮМЕ

**Актуальность.** В пост-COVID периоде у женщин репродуктивного возраста описаны нарушения менструального цикла и снижение качества жизни; опубликованные исследования неоднородны по дизайну и дефинициям.

**Цель.** Оценить взаимосвязь пост-COVID нарушений менструально-оварийной функции с качеством жизни и уровнем стресса.

**Материал и методы.** Одномоментное исследование (клиника «Шифо Нур», Ташкент). n=144: пост-COVID с нарушениями (n=62), пост-COVID без нарушений (n=52), контроль без COVID-19 (n=30). Менструальные исходы фиксировали по FIGO; стресс оценивали адаптированной IES-R (10 пунктов, 0–10; сумма 0–100).

**Результаты.** Нерегулярные менструации чаще у пост-COVID с нарушениями (72,6%, 45/62) vs контроль (30,0%, 9/30; p<0,001), OR = 6,18 (95% ДИ 2,37–16,13). IES-R:  $88,24 \pm 2,9$ ;  $73,79 \pm 2,5$ ;  $68,92 \pm 2,3$  соответственно (p<0,001 и p<0,01 vs контроль). Доля «высокого стресса» существенно не различалась (p>0,05).

**Выходы.** Пост-COVID состояние ассоциировано с большей частотой нерегулярных менструаций и более высоким стресс-бременем, особенно у женщин с жалобами на нарушения цикла. Комбинация FIGO-ориентированной оценки и краткого стресс-скрининга (IES-R) может оптимизировать маршрутизацию и наблюдение.

**Ключевые слова:** COVID-19, менструальный цикл, нерегулярные менструации, качество жизни, IES-R, психосоциальный стресс, здоровье женщин, FIGO.

COVID-19 has affected health and quality of life worldwide and remains clinically relevant in the post-acute (“post-COVID/Long-COVID”) phase for many patients. [2,5]. Among women of reproductive age, emerging evidence points to menstrual-cycle disturbances (irregularity, changes in duration and flow) and reduced health-related quality of life (HRQoL). While these signals are consistent across multiple cohorts, the literature is heterogeneous in design and outcome definitions, and confounding by age, BMI, time since infection, and cycle day is common, underscoring the need for standardized assessment and reporting. [2,3,8]. Two mechanistic domains plausibly converge on post-COVID menstrual

changes. First, psychobiological stress can alter hypothalamic–pituitary–ovarian (HPO) regulation, leading to anovulation or cycle irregularity. A 2024 systematic review synthesizing adult data found that most studies report an association between psychological stress and menstrual dysfunction, most often irregular menses and abnormal flow; the authors also highlighted inconsistencies in how “menstrual disturbance” is defined across studies, motivating better standardization in future work. Second, post-infectious endocrine–immune effects have been described, particularly involving the thyroid axis [8,9,10]. Prospective data show that after acute COVID-19 some women exhibit thyroiditis or autoimmune thyroid dis-

ease (ATD), with higher anti-TPO titers and an increased prevalence of ATD versus matched controls; other cohorts show that many acute thyroid test deviations regress by 3–6 months, though autoimmunity may persist in a subset. These findings suggest a pathway whereby HPT (thyroid) perturbations can secondarily influence HPO regulation and menstrual function in susceptible women [6,4,10].

Against this backdrop, several clinical studies published in 2024 examined menstrual alterations after COVID-19 and their correlates with mood and sleep. A prospective observational analysis reported increased menstrual changes in the pandemic context and linked amenorrhea with depressive symptoms—consistent with functional hypothalamic amenorrhea paradigms. [8,9,10]. These data dovetail with stress-focused syntheses and strengthen the rationale for pairing menstrual phenotyping with validated stress measures in post-COVID cohorts. For menstrual phenotyping itself, the FIGO systems offer a robust framework: the symptom-based system for normal or abnormal uterine bleeding and the PALM-COEIN classification for etiologies, with 2018 revisions designed to improve reproducibility across studies and clinical settings. Using these systems clarifies outcomes (frequency, regularity, duration, volume) and aligns new studies with international standards [7].

#### OBJECTIVE

To investigate how post-COVID-19 menstrual and ovarian dysfunction affects quality of life in women of reproductive age.

#### MATERIAL AND METHODS

A cross-sectional analytic study was conducted at the “Shifo Nur” clinic (Tashkent). We enrolled 144 women of reproductive age (mean age  $29.0 \pm 6.4$  years). Three groups were formed: the main group – women with a history of COVID-19 who had menstrual dysfunction ( $n = 62$ ; mean age  $22.6 \pm 3.2$  years); the comparative group – women with a history of COVID-19 without menstrual disturbances ( $n = 52$ ); and the control group – apparently healthy women without prior COVID-19 ( $n = 30$ ; mean age  $26.4 \pm 4.1$  years). The mean age at menarche in the total sample was  $13.0 \pm 2.3$  years (median 12 [11; 15]).

Inclusion criteria: reproductive age; documented history of COVID-19 for groups 1–2; absence of prior COVID-19 for the control group; no active severe somatic or psychiatric disease. Exclusion criteria: polycystic ovary syndrome and endometriosis stage III–IV; pregnancy/lactation; recent hormone therapy; acute in-

flammatory process at the time of assessment.

Clinical and questionnaire assessment included:

- a standardized menstrual function questionnaire based on FIGO criteria (frequency, regularity, duration, and volume of bleeding) with predefined outcomes: “irregular cycle” (yes/no), “menorrhagia” (yes/no), and impact on daily activity/work/sleep (categorical responses);

- an adapted short version of the IES-R (10 items; response scale 0–10) validated to assess the intensity of stress responses; total score 0–100 (higher scores indicate greater impact). Internal consistency of the scale was planned to be evaluated using Cronbach’s alpha. The survey was administered electronically with guaranteed anonymity. For groups 1–2 we additionally recorded: time elapsed since COVID-19 (months), severity of the acute illness (outpatient/inpatient), and vaccination status (yes/no).

Our primary approach was regression-based. The binary primary outcome, irregular menses (yes/no), was analysed using multivariable logistic regression; the secondary outcome, total IES-R score, was analysed using linear regression (ANCOVA). We prespecified two contrasts—“main vs control” and “comparative vs control”—and controlled multiplicity using the Holm method. Model diagnostics included multicollinearity (VIF), linearity of the logit for continuous covariates, and inspection of linear-model residuals (Q–Q plots, Breusch–Pagan test). When assumptions were markedly violated, we additionally computed bootstrap 95% CIs (2000 resamples). The significance threshold was two-sided  $p < 0.05$ . Analyses were performed in Stata

#### RESULTS

A total of 144 women of reproductive age were analyzed: post-COVID with menstrual disturbances ( $n = 62$ ), post-COVID without disturbances ( $n = 52$ ), and controls without COVID-19 ( $n = 30$ ). Age at menarche averaged  $13.0 \pm 2.3$  years (median 12 [11; 15]). Irregular menses were more frequent in the post-COVID group with disturbances (45/62; 72.6%) compared with controls (9/30; 30.0%), yielding a statistically significant difference ( $p < 0.001$ ) and a large effect size (OR = 6.18; 95% CI 2.37–16.13) (Table 1; Figure 1).

Bar chart comparing the proportion of irregular cycles in the post-COVID group with menstrual disturbances (72.6%; 45/62) versus controls (30.0%; 9/30). The contrast corresponds to an odds ratio of approximately 6.2, indicating a substantially higher risk among post-COVID patients with disturbances.

Table 1

#### Irregular menses (frequency)

Group	n	Irregular menses, n (%)
Post-COVID with menstrual disturbances	62	45 (72.6%)
Control (never had COVID-19)	30	9 (30.0%)

Menorrhagia occurred in 3/62 (4.8%) vs 1/30 (3.3%), respectively (between-group  $p > 0.05$ ). For amenorrhea, oligomenorrhea, and intermenstrual bleeding,  $p > 0.05$

in all comparisons (data not shown). Most disturbances were reported within the first 6 months after recovery.

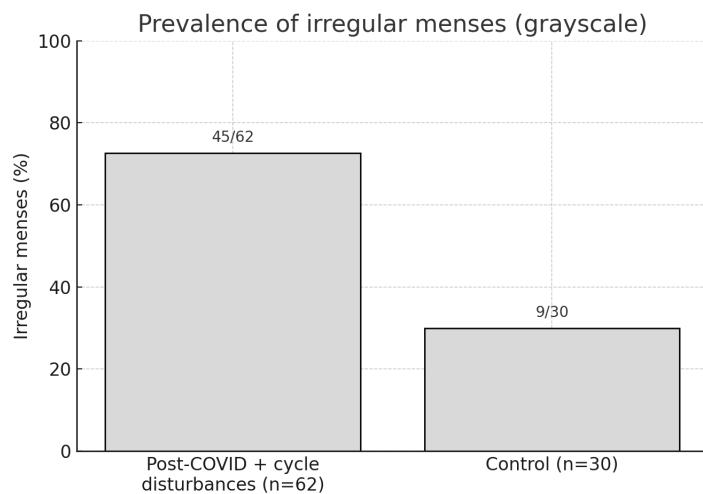


Fig. 1. Prevalence of irregular menses (%).

Psychosocial status and quality of life (IES-R). The total IES-R score (0–100) was highest in the post-COVID group with disturbances ( $88.24 \pm 2.9$ ), compared with the post-COVID group without disturbances ( $73.79 \pm 2.5$ ) and controls ( $68.92 \pm 2.3$ ). The difference vs controls was highly significant ( $p<0.001$ ); the comparison vs the post-COVID group without disturbances was not statistically

significant ( $p>0.05$ ); the post-COVID without disturbances vs controls contrast reached  $p<0.01$  (Table 2; Figure 2). The proportion of women with “high stress” (per your threshold definition) did not differ significantly across groups ( $p>0.05$ ), indicating a similar distribution of high IES-R values.

Table 2

IES-R total score (mean  $\pm$  SEM) by group

Group	n	IES-R, mean $\pm$ SEM
Post-COVID with menstrual disturbances	62	$88.24 \pm 2.9$
Post-COVID without disturbances	52	$73.79 \pm 2.5$
Control (never had COVID-19)	30	$68.92 \pm 2.3$

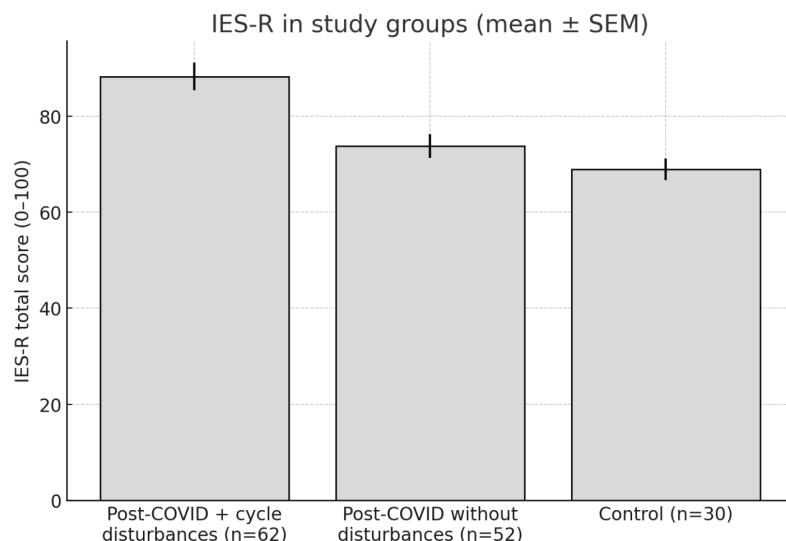


Fig. 2. IES-R scores across study groups (mean  $\pm$  SEM).

Bar chart showing higher IES-R totals in the post-COVID group with menstrual disturbances compared with the post-COVID group without disturbances and the control group. Error bars indicate SEM; higher scores reflect greater stress impact.

In this cohort, post-COVID status was associated with a markedly higher prevalence of irregular menses and with elevated stress/HRQoL burden (IES-R), particularly among women reporting menstrual disturbances, supporting integrated gynecologic and psychosocial assessment in post-COVID care.

## CONCLUSIONS

In this cross-sectional study of 144 women, a history of COVID-19 coupled with self-reported menstrual disturbances was associated with a marked excess of irregular cycles (72.6% vs 30.0%; OR = 6.18; 95% CI 2.37–16.13) and the highest stress burden on the adapted IES-R (mean  $88.24 \pm 2.9$ ). Women who had COVID-19 without menstrual disturbances showed intermediate IES-R scores and no excess of irregular menses relative to controls. This pattern supports a dual post-COVID signal–menstrual dysregulation and psychosocial distress—most pronounced in symptomatic patients.

Clinically, our findings argue for integrated assessment in post-COVID gynecologic care: (1) standardized FIGO-based phenotyping of menstrual function (frequency, regularity, duration, volume); (2) brief stress screening (e.g., IES-R short form) to identify patients with high psychosocial load; and (3) clear counseling and follow-up pathways, including lifestyle guidance, symptom diaries and, where indicated, referral for psychological support. Such a bundled approach can improve patient communication, prioritize targeted interventions, and reduce unnecessary testing.

From a public-health and research perspective, results highlight the need for longitudinal studies to clarify temporal dynamics and causality, and for multivariable models that address confounding (age, BMI, cycle day, time since infection, vaccination, comorbidities). Limitations include single-center design, self-reported outcomes, and the use of an adapted 10-item IES-R (requiring formal psychometric reporting, e.g., Cronbach's  $\alpha$ ). Strengths are the standardized menstrual framework (FIGO), explicit definition of contrasts between groups, and presentation of effect sizes with confidence intervals. Overall, the data support incorporating combined menstrual and psychosocial screening into routine post-COVID pathways for women of reproductive age.

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