

Long COVID and Perimenopause

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ABSTRACT

Coronavirus disease-2019 (COVID-19) has created a huge impact globally. It created great havoc and claimed many lives. It left a trail on those who survived. Long COVID also known as post-acute sequelae of SARS-CoV-2 infection (PASC) affects 50–70% of people who survive for 3 months or longer after acute COVID-19 infection. It is an emerging syndrome and involves multiple systems due to alterations in cellular energy metabolism and reduced oxygenation to tissues.

Keywords: Coronavirus disease-2019, Perimenopause, Women.

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INTRODUCTION

Coronavirus disease-2019 (COVID-19) has created a huge impact globally. It created great havoc and claimed many lives. It left a trail on those who survived. Long COVID also known as post-acute sequelae of SARS-CoV-2 infection (PASC) affects 50–70% of people who survive for 3 months or longer after acute COVID-19 infection.¹ It is an emerging syndrome and involves multiple systems due to alterations in cellular energy metabolism and reduced oxygenation to tissues.

Individuals who have suffered from COVID-19 infection can have persistent signs and symptoms which can affect the quality of life. The symptoms may be related to neurocognitive, cardiorespiratory, gastrointestinal, and musculoskeletal systems. Along with affection of these systems other symptoms like loss of taste and smell can be present.²

Perimenopause or menopausal transition period is the period for years prior to menopause causing various symptoms which affect the quality of life in women. There is a depletion of ovarian follicles leading to decreased estradiol production. Perimenopause is marked by cycle irregularity, vasomotor symptoms, and many more symptoms.

Symptoms like fatigue, cognitive issues (often referred to as brain fog), and heightened heart rate following recovery from COVID-19 can persist or worsen over time, characterizing long COVID.³ Long COVID and perimenopause share similar symptoms such as hot flashes, night sweats, poor sleep, mood changes, emotional lability, depression, anxiety, brain fog or decreased concentration, decreased stamina, fatigue, joint and muscle pains, and headaches. It is very difficult to differentiate whether symptoms are due to long COVID or perimenopause as there is no single test to diagnose long COVID.

REVIEW OF LITERATURE

A meta-analysis and review of multiple studies pinpointed female sex and the severity of acute illness as primary risk factors for long COVID, contrasting the mortality risk factors for acute COVID-19 which involves age, male sex, and chronic conditions.⁴ The increased occurrence of long COVID among women under 50-years-old suggests a potential link between symptoms of

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long COVID and perimenopause. Perimenopause might be misdiagnosed as long COVID or these two conditions might mutually influence each other.

The overlap of symptoms of long COVID and perimenopause have been supported by studies where it was observed that there is a high prevalence of long COVID in women younger than 50 years, considering the median age of menopause as 51 years.^{4–6}

In women with long COVID infection inflammatory markers are elevated for several months.⁷ This chronic inflammation potentially disturbs ovarian function and hormone production.^{7–9} During perimenopause, the ovaries become more vulnerable to illnesses like COVID-19 and stress. One theory suggests that COVID-19 could impact ovarian function, leading to declines in ovarian reserve, disturbances in the menstrual cycle, and gonadal function and potentially affecting menopause or fertility along with exacerbation of symptoms around menstruation.^{6,10} The virus might affect hormone production due to the abundance

of angiotensin-converting enzyme- receptors in ovarian and endometrial tissues.⁹

Given these impacts, it is plausible that long COVID could intensify perimenopausal or menopausal symptoms or prolong their duration. Gender differences have been observed in symptomatic COVID-19, with women generally experiencing milder symptoms.^{11,12} Estradiol, a form of estrogen has shown positive effects during active COVID-19 infection, potentially contributing to lower mortality rates among women, reduced inflammation, higher lymphocyte counts, and faster antibody responses compared to men.^{11–13} Additionally estradiol has been known to alleviate symptoms like hot flashes, night sweats, and mood disturbances during perimenopause.¹⁴

Perimenopausal women who have suffered from COVID-19 infection and present with persistent symptoms without any other alternative diagnosis and have menstrual irregularity, hot flashes, or night sweats are perhaps suffering from an exacerbation of perimenopausal symptoms or could be experiencing a combination of long COVID and perimenopause.¹⁵

It is crucial to distinguish between perimenopause and long COVID, as individuals might experience both concurrently, potentially intensifying perimenopausal symptoms.^{3,6} Women may have menstrual irregularity along with poor sleep, hot flashes, and mood swings. If women going through perimenopause report to a healthcare professionals with sudden worsening of symptoms post COVID, healthcare providers should address these symptoms and assess whether hormonal therapy will alleviate these symptoms. Women do not necessarily wait for a year without a menstrual cycle to start hormonal therapy. If required healthcare providers should start a combination of estrogen and progesterone under close follow-up.¹⁶ Other non-hormonal treatment options also can be considered.

Regarding potential interventions, a recent retrospective case-matched study discovered that individuals with long COVID exhibited lower levels of 25 (OH) vitamin D 66 months after hospital discharge with brain fog being a notable symptom.¹⁷ This finding suggests a potential role of vitamin D supplementation as a preventive measure for individuals being discharged after hospitalization. However, beyond this observation, the assessment of vitamin D levels and supplementation for long COVID remains unexplored.

What Can We Do?

Health care providers should encourage lifestyle modifications in women experiencing perimenopause and long COVID. It includes good nutrition with emphasis on proper protein intake, following proper sleep habits with at least 7 hours of sleep, doing yoga and meditation, and regular exercise at least 5 days a week.

The period of menopause may also coincide with midlife stressors such as divorce or separation, health issues of partner or family elders, parenting demands, midlife career, and so forth. These stressors collectively heighten the challenges associated with both long COVID and perimenopause, making navigation through this period more demanding. Hence health care providers should also pay attention to mental health issues. Proper listening to their problems and counseling is required in these women. We should encourage them to do yoga and meditation and if required help of a psychologist or psychiatrist should be taken.

If symptoms are not relieved by lifestyle modifications, the health care provider should decide on hormone therapy after

thorough history taking, proper examination, and doing necessary investigations. It is very important to rule out contraindications for hormonal therapy.

CONCLUSION

Symptoms of long COVID and perimenopause may be overlapping or perimenopausal symptoms may get exacerbated in women with long COVID. Healthcare providers should keep these two conditions in mind and help women tide over this phase by advising proper lifestyle modifications, tackling their mental issues, and prescribing them with non-hormonal and hormonal medications.

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