

# Does COVID-19 Infection Affect Female Reproductive System?



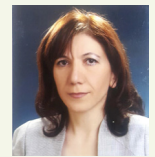
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Starting in December 2021, in the city of Wuhan, China, and spreading rapidly all over the world, SARS-CoV-2 (COVID-19) has led to an increase in morbidity and mortality all over the world. The most common findings are fever, sore throat, and myalgia. Although clinical findings can be mild sometimes, symptoms can be serious enough to cause death, such as severe acute respiratory syndrome (SARS) (1). One of the mechanisms held responsible for the multiorgan complications of COVID-19 is its entry into the cell via angiotensin converting enzyme-2 (ACE2) (2). The S protein of the virus binds to ACE2 receptor of the host cell, and this complex is exposed to proteolytic processing by the host type II transmembrane serine protease (TMPRSS-2) enzyme and the virus enters the cell (3). Therefore, tissues with high ACE2 receptors may be more sensitive to this virus. The presence of these receptors in ovarian granulosa cells has been demonstrated in previous animal studies (4). Moreover, the importance of ACE2 in human ovary has been shown (5, 6).

On the other hand, the uterus, especially endometrium, has pivotal role in fertility and, components of the renin-angiotensin system (RAS) are found in epithelial and stromal cells of endometrium (7). Furthermore, viral entry is dependent on primary cleavage of the S protein, which cleavage can be activated by one or more host proteases, including FURIN, trypsin, cathepsin, TMPRSS-2, or TMPRSS-4 (transmembrane serine protease 4) (3). In human endometrium, the expression of proteases such as TMPRSS4, CTSA (Cathepsin A), CTSB (Cathepsin B), CTSL (cathepsin L), BSG (basigin), FURIN, and MX1 has been shown to vary in different phases of the cycle in both natural and controlled ovarian stimulation cycles. It has also been found that this expression increases with age. For this reason, it has been stated that the endometrium and implantation may be affected by the virus more specifically with age (8, 9). Therefore, Covid-19 may affect endometrium and implantation (10).

In various studies, transient menstrual changes, usually in the form of prolonged cycles and reduced

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bleeding volume were observed in patients infected with COVID-19 (11-13). In a small group of patients, shorter or disordered menstrual cycles, and heavy menstrual bleeding were observed compared to the control group. Changes to menstruation did not vary with the severity of the disease and generally returned to normal within a few months of follow-up (12). Changes in anti-Mullerian hormone (AMH) and the other hormone levels are currently unclear in the literature (12,13).

All these menstrual changes may be due to the stress caused by the disease or the direct effects of the virus on the ovary and endometrium. This whole process may adversely affect fertility and ovarian reserve. However, current data are very limited and additional studies are needed.

## Ethical Issues

Not applicable.

## Conflict of Interests

The author has no conflicts of interest to disclose.

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