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THE EFFECTS OF THE POST-INFECTION OF COVID-19 ON MENSTRUAL CYCLE IN WOMEN

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Abstract

Introduction*: COVID-19 is a virus that negatively affects the population in several factors, varying from signs and symptoms that cause infection in several organs of the body. In regard of these infections, there are several permanent and temporary sequelaes on people, some of them are correlated with hormonal and ovarian changes, causing irregularities in the menstrual cycle of women after being infected by the virus.* ***Objective:*** *In this context, we intend to investigate the main impacts of COVID-19 on the menstrual cycle on women.* ***Methon:*** *Study was based on the qualitative narrative literature review methodology, in search for a critical analysis of the literature.* ***Result:*** *This research pointed out that COVID-19 enters through the respiratory system, binds to ACE2, an enzyme in which it is present on the ovarian and endometrial tissues and affects the production of ovarian hormones and alters the endometrial response during the menstrual cycle.* ***Final considerations:*** *Through this research, we identified that women after the COVID-19 infection, there was changes on the period of the menstrual cycles such as: amenorrhea, increased blood flow, exacerbation of menstrual cramps, change in the duration of the menstrual period, developing symptoms of fatigue, back pain, insomnia and fatigue. Women who have become and still become hostages of cultural taboos of restrictions, segregation and discrimination, constantly changing their lifestyles.*

Keywords: *Women, Menstrual Cycle; Infection; COVID-19.*

1. INTRODUCTION

One of the first infections caused by COVID-19 was first reported in December 2019 in Wuhan, China. Since then, the COVID-19 contamination rate has been gradually increasing every day around the world, influencing changes in people's routines, especially in health services, such as UBS, UPA and hospitals. (BRAZÃO; NÓBREGA. 2021)

COVID-19 infection has resulted in serious health problems, especially affecting all organs and systems, especially respiratory diseases. Campos et al. (2020) state that the etiological agent SARS-CoV-2, upon entering the host organism, binds to the angiotensin-converting enzyme 2 (ACE2) receptor, allowing entry into the target cell and replication, triggering an immune response in the host, with the first symptoms and clinical manifestations appearing.

The immune system works in defense by fighting infectious agents. This function is initially mediated by the reactions of innate and late immunity, adaptive immunity, characteristics in the fight against viral infections.

The severe form occurs in a portion of patients who manifest a marked immune response to SARS-CoV-2. Human cells, when infected by viruses, are recognized by immune systems that initiate the production of cytokines[1].

One of the conditions affected by COVID-19 in women is the alteration of the menstrual cycle after infection. Under these conditions, there are many factors that can lead to the alteration of the menstrual cycle such as stress, nutrition, infections, endocrine, gynecological, autoimmune, genetic and lifestyle changes. According to Taskaldiran et al. and Derevechi (2022), it was observed that some women had irregularities in menstruation after COVID-19 infection. The menstrual cycle is the phenomena that occur in the uterus in order to receive the fertilized egg, therefore, during the period in which this phenomenon occurs, several changes occur in the daily life of a woman, causing her to have another view of life during the period. This phenomenon affects the psychological, social and cultural dimensions of women.

According to Cherenack et al. (2022), in the city of Shanghai, China, some women hospitalized due to COVID-19 infection showed the occurrence of interruptions in menstrual cycles after infection, consisting of low menstrual volume (20%) and long menstrual cycles (20%), and it was proposed that changes in the menstrual cycle may be associated with the presence of specific proteases in the female reproductive system and the ability of the virus SARS-CoV-2 from infecting endometrial cells.

According to Taskaldiran et al. (2022), it was observed that the viral infection of COVID-19 itself can alter the menstrual cycle. The SARS-CoV-2 virus enters the cell by binding to the ACE2 receptor (angiotensin-converting enzyme 2). It was previously found only in the respiratory tract but now known to be found in the ovary and endometrium as well.

According to Thiesen et al. (2022), they report that ACE2 receptors have a gateway to COVID-19 infection, receptors that are present in ovarian and endometrial tissue, where they help alter the production of ovarian hormones and/or the endometrial response during menstruation.

As a result, our research had the problem of discussing the extent to which COVID-19 impacted the menstrual cycle in women. Raising as a hypothesis that women are more susceptible to presenting hormonal changes related to the cycle after COVID-19 infection. The general objective is to evaluate the possible impacts of post-infection of COVID-19 on the menstrual cycle in women.

2. METHODS

This work is a qualitative narrative literature review study, characterized by not using explicit and systematic criteria for the search and critical analysis of the literature. According to Rother (2007), the narrative review describes, discusses and develops the "state of the art" of a given subject, from a theoretical or contextual point of view.

During the development of this study, we used about seven articles, three books, three health journals and three websites with a focus on health related to our theme. Basically, we use the analysis of the literature published in books, articles from printed and/or electronic magazines in the interpretation and personal critical analysis of the author, in the languages in English, Spanish and Portuguese. The inclusion criterion was content/studies carried out between the last five years (2019–2023). This study model is widely used in the development of dissertations, theses, course completion works and for the theoretical foundation of articles.

The search base of this study was carried out through the tools: Scielo, Virtual Health Library, GOOGLE SCHOLAR, physical books and health-based journals. The search strategy will be through the search of the following descriptors: "Women", "COVID-19" and "SARS-CoV-2". Through these sources, articles, books and magazines with the proposed themes were found.

3. THE FLOWS OF THE MENSTRUAL CYCLE AND THEIR IMPACTS ON THE BODY

Menstruation is the biological process of desquamation of the inner walls of the uterus that happens in women, when there is no fertilization related to the monthly production of estrogens and progesterone by the ovaries. According to *Santos (2018),* this process is made up of phenomena that occur in the uterus and is related to the preparation of the endometrium, where it is an inner layer of the uterus, to receive the fertilized egg. If fertilization does not occur within 2 days before the end of the monthly cycle, the corpus luteum in the[2] ovary involutes, and the secretion of ovarian hormones decreases, thus the endometrial layer is dissolved and menstruation occurs, which starts a new menstrual cycle. This period lasts about 28 days and can vary between 24 and 35 days or irregularly.

According to Lasta et al. (2022), excessive menstrual variations are characterized by an amount of bleeding greater than 150ml and/or duration greater than 7 days and/or menstrual intervals of less than 21 days. Alterations due to the absence of bleeding involve primary and secondary amenorrhea, with primary amenorrhea associated with the absence of menarche at 14 years of age, accompanied by the absence of development of secondary sexual characteristics at 16 years of age. In the case of secondary pregnancy, it involves a lack of menstruation for 6 or more months after the discarding of a possible pregnancy.

Dysmenorrhea comprises painful changes, which can be primary or secondary to previous diseases, such as endometriosis or infections. The pain is usually spasmodic, intense in the hypogastric region, managing to radiate to the back and thighs, starting a few hours or days before menstruation and lasting from 2 to 7 days.

> The hormonal cycle is the phase in which the natural regulation of hormones occurs. Although estrogens and progesterone are produced in the ovary and uterus, luteal-stimulating (LH) and follicle-stimulating (FSH) hormones are produced in the adenopituitary gland, are present in all phases of the female reproductive cycle but are characterized by moments of greater or lesser production during the cycle. (GUYTON e HALL, 2021)

[1]**Cytokine**: Generic name for certain substances secreted by cells of the immune system that control the body's immunoreaction.

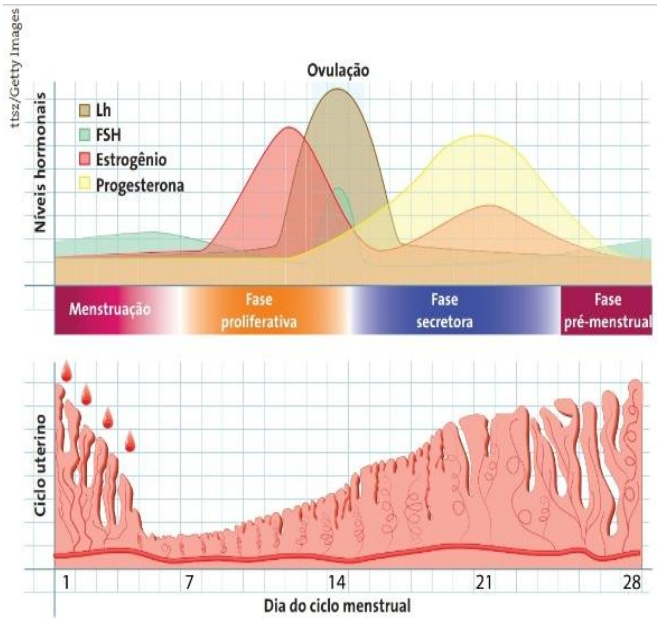
[2] **Corpus luteum:** A temporary endocrine gland formed after ovulation.

According to Santos (2018), the ovary goes through three phases. Menstrual phase**,** also called follicular phase or menstruation, in this period, the concentration of follicle-stimulating hormone rises slightly, influencing the development of several follicles in the ovaries, each follicle has an egg. This period, which is marked by bleeding or hemorrhage, lasting an average of 3 to 5 days, in this phase, in addition to blood loss, there is a loss of cells from the inner layer of the uterus.

Pre-ovulatory phase, called the proliferative or ovulatory phase, defined by the expansion of the inner wall of the uterus doubling in size and the appearance of new blood vessels that prepare the uterus for fertilization, estrogen levels continue to rise and produce luteinizing hormone (LH) in which it is in charge of selecting mature eggs and transporting them to fertilization. Luteinizing hormone stimulates the release of the egg (ovulation), which typically occurs 16 to 32 hours after the cycle begins. The concentration of estrogen decreases during the cycle, and the concentration of progesterone begins to rise.

Post-ovulatory phase, which can also be termed as secretory or luteal phase, is an uninterrupted phase, lasting about 14 days, defined by the elevation of glycogen and blood vessels. There is a decrease in the concentration of luteinizing hormone and follicle-stimulating hormone. During most of this phase, the concentration of estrogen is high. Progesterone and estrogen cause the lining of the uterus to become even thicker, to plan for probable fertilization.

Figure 1: Menstrual cycle: phases and hormones.



Source: Nursing in Gynecology and Women's Health.

The menstrual cycle brings a series of changes in a woman's lifestyle, and for many women it is not just a period in which they feel cramps, but a period in which the body develops various signs and symptoms such as, for example, psychological symptoms that include irritability, aggression, tension, anxiety and depression, changes in appetite that possibly interfere with the ability to concentrate, reasoning and social life. In addition, the body develops somatic changes such as edema, breast tenderness, headache and weight gain.

As all women menstruate, they become hostages to the same social, cultural taboos of restriction, segregation and discrimination. Many adolescents and women are unable to purchase some type of disposable daily pad, so the United Nations Population Fund (UNFPA) and the United Nations Children's Fund (UNICEF), work to guarantee the rights of each child and adolescent, based on the document *"Menstrual Poverty Experienced by Brazilian Girls"* described that menstrual poverty refers to numerous challenges in accessing rights and health supplies. Challenges in which they represent, for girls, women, trans men and non-binary people who menstruate, unequal access to rights and opportunities. The lack of knowledge about menstrual health care can affect even people who are not in poverty. They may face the lack of adequate products for menstrual hygiene, considering the disposable pad as a superfluous product.

There is little information regarding the reasons that trigger these signs and symptoms in women during the menstrual period, however, it is believed that socioeconomic and social factors, such as lifestyle, use of medications, smoking, alcohol consumption and lack of physical exercise can contribute to the appearance and worsening of symptoms before and during this period.

4. CHANGES IN THE MENSTRUAL CYCLE AFTER COVID-19 INFECTION

COVID-19 is a pathology caused by the SARS-CoV-2 virus, which negatively affects infected individuals in several factors, ranging from mild to moderate or severe symptoms. As a result of the infection, several sequelae occur, which persist indefinitely.

According to Cherenack et al. *(2022),* hormonal and metabolic changes (as occurs in polycystic ovary syndrome) and inadequate nutritional intake (in the context of high energy expenditure, which can be differentiated by social constructions, such as race or income), can cause changes in menstruation. New research indicates that menstruation may also be stopped during the SARS-CoV-2 virus pandemic. Therefore, it is not known for sure to what extent this cessation resulted in stress, mental health change, COVID-19 infection, and/or SARS-CoV-2 vaccination.

According to Lasta *et al.* (2022), COVID-19 is responsible for pulmonary and extrapulmonary changes. Among the changes that occur outside the lung region are vascular and endocrine changes that can lead to a prothrombotic state, hyperglycemia and ketosis. These extrapulmonary infections may be related to hormonal and ovarian changes that possibly affect the menstrual cycle of women after COVID-19 infection. Thus, we hypothesized that COVID-19 infection can cause direct or indirect changes in the menstrual cycle, influencing the increase or decrease in flow, cycle length, and presence of pain.

COVID-19 can provoke an excessive immune reaction, raising the level of cytokines, produced by activated leukocytes, activating the inflammatory cascade, causing great damage to different tissues. Possibly, this excessive activation of the immune system is the cause of most organic manifestations (cardiomyopathy, nephropathy, etc.), including neurological ones. Severe cases of COVID-19 are more prone to manifestations of severe neurological syndromes. Another situation to be considered is the endothelial dysfunction caused by SARS-CoV-2, causing AMI (acute myocardial infarction) and hemorrhages, which can occur in different organs, becoming, in turn, to dominate the clinical picture, with AMI, renal complications, digestive bleeding and stroke.

COVID-19 infection is based on the initiation of the respiratory system due to the higher concentration of angiotensin-converting enzyme-2 receptors. This enzyme plays a fundamental role in the ovary where the secretion of steroids is promoted, which help in follicular development and oocyte growth, influencing ovulation while maintaining the function of the corpus luteum.

COVID-19 infection can affect the hypothalamic-pituitary-ovarian axis[3], resulting in hypothalamic hypogonadism (low estrogen and progesterone production), which can lead to temporary or permanent menstrual irregularities. (TASKALDIRAN, et al. 2022).

However, a healthy woman's menstrual cycle usually lasts 25 to 30 days and can vary from woman to woman. When the cycle length is shorter or longer, it is considered an irregular cycle. Therefore, to be proven that it is a regular cycle, there is no need to always occur with the same duration, but with a similar interval over the months.

In agreement with Taskaldiran *et al.*, angiotensin-converting enzyme-2 receptors have been observed to be present in both ovarian and endometrial tissue, and therefore COVID-19 infection can affect ovarian hormone production and endometrial response during menstruation. For example, the change in the number of leukocytes in the endometrium during or after COVID-19 infection. Immune activation induced by viral infection is related to exacerbation of premenstrual symptoms associated with progesterone. As a result, SARS-CoV-2 infection was also associated with endothelial cell dysfunction and changes in the coagulation system, both critical components of endometrial function during menstruation, indicating a potential endometrial mechanism for menstrual disorders.

In addition, ACE2 receptors are widely expressed in the ovaries and endometrium, suggesting that SARS-CoV-2 infection affects the hypothalamic-pituitary axis, which can cause menstrual irregularities by directly affecting the ovaries and endometrium.

According to the endocrinologist and the president of the Brazilian Diabetes Society of Paraná (SBD-PR) André Vianna, they claim that studies are still beginning to appear proving a direct relationship between changes in menstrual flow and Covid-19 and explains that the virus also affects the hormonal system indirectly, through the pituitary gland. (HOSPITAIS BRASIL-PUBLIMED Magazine, 2021)

In this sense, the physiological process according to the menstrual regulation cycle, women are more likely to show a better response to infections both at the humoral and cellular immune levels. These manifestations may be related to differences in estrogenic and androgenic hormone levels between the sexes, as estrogen and testosterone bind to receptors of immune activity cells. It is known that estrogen is involved, when at high levels, with the suppression of the innate immune response and when at low levels, it is related to immunostimulant activity (OLIVEIRA, 2020).

5. FINAL CONSIDERATIONS

This work was committed to understanding the impacts of post-COVID-19 infection on the menstrual cycle. With this, this study becomes extremely important for women who seek this type of information, in order to know the hormonal changes that occur in the body during the menstrual cycle after a SARS-CoV-2 viral infection.

Generally, menstruation is a regularly overlooked health indicator in infectious disease studies. The relationship of COVID-19 infection to menstrual irregularities highlights the need for specific research to assess menstruation during the pandemic to better understand how SARS-CoV-2 infection, stress, and mental health can modify women's health.

Sources of research under development have found that COVID-19 has a means of entry through ACE-2, present in ovarian and endometrial tissue that alters the production of hormones (LH and FSH). Hormones in which it has the function of producing follicles, promoting ovulation and producing estrogen and progesterone, are the main triggers of menstruation. With this change, the menstrual cycle is modified. The main changes in the menstrual cycle are the exacerbation of cramps, change in the length of the period, and the regular period usually happens in an average of 28 days.

Other alterations found were the triggering of signs and symptoms such as stress, anxiety, nervousness and insomnia and even hypermenorrhea and amenorrhea. Therefore, there are several factors that can have consequences on the menstrual cycle, such as stress, nutrition, genetics, infection, changes in the endocrine, gynecological, autoimmune system, and lifestyle changes.

Considering that SARS-CoV-2 affects several systems, including the immune, endocrine, and neurological systems, the treatment and care propositions for women infected by COVID-19 and had menstrual manifestations are, the adequacy of a healthy life, adequate water intake, ensuring necessary nutrients for the brain, immune system, and cardiac. Consume substances such as omega 3, vitamins, magnesium, and selenium. As well as the use of medications, such as analgesics and antipyretics, or interventions established by the health team depending on the need. One of the forms of prevention is vaccination, use of a protective mask, hand hygiene, avoiding crowds and avoiding touching the eyes, mouth and nose.

During the menstrual period, many women report cramps to relieve symptoms. We can consider pharmacological measures such as the use of analgesic or anti-inflammatory drugs, which will partially or completely eliminate pain. Treatment can also be done by non-pharmacological measures, such as physical exercise, a healthy diet rich in fiber, application of a warm compress in the lower abdomen, relaxation techniques and home remedies such as teas.

Based on the analysis of several studies, it is concluded that there is still ongoing research that seeks to prove a direct relationship between changes in menstrual flow and COVID-19. The development of this study allowed us to clarify doubts about the theme initially proposed, highlighting its relevance for a deeper understanding of this theme.

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