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The Effects of COVID-19 from Fertilization until Birth: A Literature Review

Seyedeh Nasim Mirbahari[1], Rahim Ahmadi[*2]

[1]Reproductive Biomedicine Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran
[*2]Avicenna International College, Budapest, Hungary

Corresponding Author Address: Hamedan Branch, Islamic Azad University, Hamedan, Iran

Tel: 0098-9120394326

Email: Rahahmadi2001@yahoo.com

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Abstract

Background: Due to the presence of the main receptor of SARS-CoV-2 (ACE2) in the male and female reproductive systems, infertility and viral damage during pregnancy are possible, in addition to premature birth, abnormal birth, and even maternal death.

Objectives: This study aimed to review the effects of COVID-19 from fertilization until birth.

Methods: By searching relevant keywords, a total of 205 articles were retrieved, 62 of which were finally reviewed in this study. Also, the Fertility Society of Australia (FSA), European Society of Human Reproduction and Embryology (ESHRE), and Human Fertilisation and Embryology Authority (HFEA) websites were checked to find reports on infertility management during the COVID-19 pandemic in other countries.

***Results*:** The coronavirus receptor (ACE2) is expressed in the tissues of the male and female reproductive systems, as well as various embryonic stages. The fetus is most likely to be infected by the virus at the time of birth. However, there are few reports of vertical transmission from the mother to the fetus before birth. Couples are generally suggested to freeze their embryos after the COVID-19 pandemic is eradicated.

Conclusion: Considering the presence of the new coronavirus receptors in the male and female reproductive systems, besides reports on the destructive effects of this virus on different parts of the male and female reproductive systems, COVID-19 can harm the next generation, as well as the current world population. Therefore, couples are advised to avoid pregnancy during the COVID-19 outbreak. In the case of pregnancy, they are asked to observe the health protocols as much as possible to prevent the spread of disease.

Keywords: COVID-19, reproductive system, pregnancy, fertilization, vertical transmission, embryo, infertility treatment, birth

Introduction

In December 2019, the first case of coronavirus disease (COVID-19) was reported in Wuhan, China. Severe infection and persistence of the virus on surfaces led to the spread of COVID-19 around the world. On March 11, 2020, COVID-19 was introduced as a global pandemic. This disease has several symptoms, including fever, cough, and shortness of breath. In some patients, the symptoms can be more severe, such as diarrhea, liver damage, and even death [1]. The new coronavirus is a large single-stranded RNA virus with a size of 32 kb that contains an envelope [2]. The envelope of this virus consists of lipids and three proteins, including the membrane, envelope, and spike proteins. The reason for the crown-shaped appearance of this virus under electron microscopy is the presence of spike proteins [3].

Infection with the COVID-19 virus is normally acute in the upper respiratory tract. The virus receptor is a protein called angiotensin-converting enzyme 2 (ACE2), which is predominantly present in the upper respiratory tract. ACE2 is also one of the recipients of severe acute

respiratory syndrome (SARS) virus, which caused an epidemic in 2003. The gene sequence of the new coronavirus has 85% homogeneity to the gene sequence of the SARS virus and 76% similarity in amino acid sequences [4]. The similarity between these two viruses suggests that COVID-19 uses a similar pattern to the SARS virus to enter the cells, but possibly with a stronger connection and higher affinity. The damage caused by COVID-19 in different organs depends on the level of ACE2 expression. ACE2 belongs to the angiotensin-converting family of dipeptidyl carboxydipeptidases, with considerable homology to ACE1 [5]. Previously, ACE2 was considered as a marker to measure blood pressure and heart rate. However, today, this protein is used as a marker to determine the vulnerability of different tissues, as well as different individuals to COVID-19 [6].

The COVID-19 pandemic is a cause of concern for various groups, especially pregnant women who are normally required to visit obstetrics and gynecology clinics, to monitor their fetal health. On the other hand, frequent physician visits can increase the risk of contracting the disease in the parents. Also, the birth of newborns in hospitals can be associated with the risk of contracting the disease. So far, studies on the transmission of COVID-19 to the fetus have been controversial. Therefore, in this study, we aimed to investigate the impact of COVID-19 from fertilization until birth.

Methods

The effects of COVID-19 on male fertility, female fertility, fetal outcomes, infertility treatment, embryo, pregnancy, fertilization, vertical transmission, and cryopreservation were investigated by searching relevant keywords in the titles of articles published in PubMed, Google Scholar, and Science Direct databases. We retrieved a total of 205 articles without any time limitations. Non-English and irrelevant papers, as well as articles without a full manuscript, were excluded, reaching a total of 112 articles. All included studies were downloaded and entered in Endnote 2017.

All selected papers were first reviewed, and after reading the full-texts, 59 articles remained in our study. The remaining articles were then categorized into nine separate groups. The articles in each group were read more carefully and summarized. While writing the main part of the article, new points were added from each article. Three new articles were also retrieved from the reference lists of the selected papers (62 articles). Moreover, to report on infertility management during the COVID-19 pandemic in other countries, reliable websites, such as the Fertility Society of Australia & New Zealand (FSA), Human Fertilization and Embryology Authority (HFEA), and European Society of Human Reproduction and Embryology (ESHRE) were checked. Finally, 65 articles were included in our review.

Results

1. Male reproductive system

Some scholars believe that there is no reason to assume that men are more likely to be infected with COVID-19 than women. However, according to a study from Southeastern China, blood estrogen levels were inversely related to the ACE2 activity and expression, which is probably the reason why women are more resistant to COVID-19 [7,8]. Previously, it was discussed that ACE2 is the main receptor of coronaviruses. ACE2 is also the main receptor of SARS virus, which also affects the spermatogonia cells [9]. The high expression of ACE2 gene in four main cell categories, that is, Leydig cells, ferrous seminiferous tubular cells, spermatogonia, and Sertoli cells of human testes, allows the virus to be present in the semen [5]. In a previous study, the expression profile of ACE2 gene was determined in different testicular cells, using two Gene Expression Omnibus (GEO) and Sequence Read Archive (SRA) databases, as shown in Figure 1.

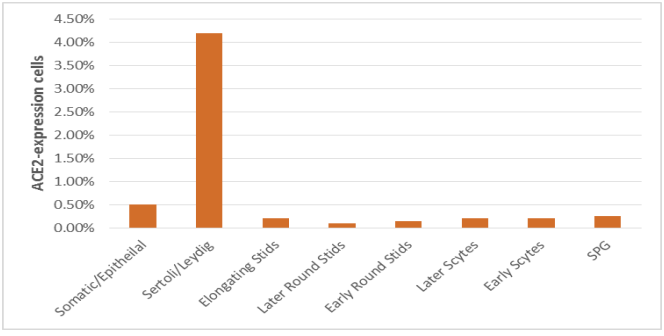

Figure 1: The ACE2 expression in each identified male germ cell type [10]

The ACE2 expression is age-dependent, with maximum expression at age 30 and minimum expression at age 60. This suggests that younger men are more likely to have testicular damage caused by COVID-19. The tissue damage in COVID-19 is caused by the virus attachment to ACE2 receptors and inflammation [10]. Generally, the semen fluid can be a suitable site for viruses. The coronavirus is similar to viruses, such as Ebola virus, which can remain in the semen culture even 2-3 months after the blood test is negative. At the time of the Ebola outbreak, couples were suggested to avoid unprotected intercourse for three months after the blood samples were negative [11]. Also, Zika virus, which is transmitted by mosquito bites in endemic areas, spread in 2015, causing encephalitis, brain disease, and Guillain-Barré syndrome in the fetus. The receptor of this virus is located on the surface of cells, and the virus enters the cells via cholinesterase-dependent endocytosis. It can remain in the semen two months after the blood test is negative [12]. There are also reports of Zika virus persisting in the semen up to a year after the symptoms have subsided [13].

On the other hand, another study reported that the nCOV RNA test of semen was negative in a 34-year-old Chinese man one month after the definitive diagnosis of COVID-19 by an oral swab [14]. In another study in Wuhan, China, on 12 men aged 22-38 years, including 11 patients with acute symptoms, the results of nCOV RNA immunoassay for the semen and testicular fluid were negative at 14 days after the definitive diagnosis of COVID-19 [15]. Similarly, a previous study showed that the presence of nCOV RNA in the semen and testicular fluid was negative in a 31-year-old man eight days after definitive diagnosis through RT-PCR testing [16]. Moreover, another study was performed in Wuhan, China, on 112 patients aged 23-83 years. In this study, 27 days after the diagnosis of COVID-19, the nCOV RNA test of the semen was found to be negative. However, in three patients with severe symptoms, testicular orchitis was observed for three days [17].

Fever can also affect the process of spermatogenesis and has been shown to reduce sperm motility and concentration after 72-90 days, resulting in a reduction in male fertility [18]. Another study from Wuhan, China, compared the sex hormones between 81 men with COVID-19 (aged 20-54 years) and 100 healthy people with a normal reproductive status via hormonal tests. This study, which was performed using electrochemiluminescence immunoassays, found that the patients' luteinizing hormone (LH) and prolactin levels increased significantly as compared to normal individuals. Although the levels of testosterone and follicle-stimulating hormone (FSH) were not significantly different from normal patients, the ratio of testosterone to LH and the ratio of FSH to LH significantly reduced in COVID-19 patients as compared to healthy individuals [19].

2. Female reproductive system

ACE2 is a significant regulator in the physiology and pathology of the male and female reproductive systems; therefore, defects in ACE2 genes and proteins can impair fertility [20]. In this regard, a bioinformatics study, based on the Gene Expression Omnibus (GEO) database, showed that ACE2 was highly expressed in the uterus and placenta, according to a single-cell RNA sequence

analysis [21,22]. The presence of ACE2 markers in the endometrium and epithelial cells of the uterus has also been confirmed in other reports. The expression of ACE2 changes during the female menstrual cycle, and its expression in the secretory phase is greater than the proliferative phase; the cause of this change may be angiotensin II hemostasis and endometrial regulation. This alteration in the expression level of ACE2 is likely to lead to a change in the vulnerability of the female reproductive system [23]. Previous studies have confirmed the expression of ACE2 in mouse and cow granulosa cells. The expression of ACE2 in these cells is regulated by gonadotropins [24]. It should be noted that there have been many reports of preterm birth, miscarriage, and intrauterine growth restriction in SARS patients [25].

3. Fertilization

So far, there have been no reports of COVID-19 transmission through blood or sexual intercourse [26]. Some evidence suggests that members of the coronavirus family have similarities to the family of viruses responsible for orchitis. Since orchitis viruses are present in the testicular epithelium and can lead to testicular damage and decreased gamete formation, SARS-CoV-2 may be present in the semen and transmitted through it [27]; this may occur in asymptomatic patients and affect their sexual partners. Although this mode of transmission for Ebola and Zika viruses was first rejected, it was later approved [11, 28].

Moreover, the presence of ACE2 receptors in various testicular tissues, as discussed in previous sections, can make the testis and semen suitable sites for SARS-CoV-2. However, the Centers for Disease Control and Prevention (CDC) rejected the presence of this virus in non-respiratory fluids [29]. Nevertheless, in Italy, infertility treatment centers ask all donors about the presence of respiratory symptoms and/or any recent travels to high-risk areas before giving gametes. To donate gametes and ensure their health, there must be a two-week interval from the elimination of respiratory symptoms [30].

4. Fetal outcomes

To examine the effects of COVID-19 on the human fetus, it is important to determine whether the ACE2 receptor is expressed in embryonic cells. Apart from ACE2, other studies have shown that SARS-CoV-2 S protein enters the cell via transmembrane protease serine 2 (TMPRSS2) [31]. Another endosomal protease, called cathepsin L (CTSL), helps the virus enter the cell [32]. Also, SARS-CoV-2 uses Basigin (BSG or CD147) as a receptor [33]. Considering the high prevalence of COVID-19 and the fact that many patients are asymptomatic carriers, pregnant women may become ill during their visits to clinics. There is also another type of fetal infection in infertility clinics, as gametes or embryos may be exposed to the virus on the clinic shelves. It is known that the high persistence of the virus on surfaces increases the likelihood of COVID-19 infection [34].

It is important to investigate the viral damage to the fetus, as these lesions can cause death or underdevelopment in different stages of embryo development [35]. In a study from India, the single-cell RNA sequence information of genes for coronavirus receptors, including ACE2, TMPRSS2, CTSL, and BSG, was analyzed in embryonic cells in various stages. Also, to investigate the entry of the virus into the cell, the simultaneous expression of each gene (TMPRSS2, CTSL, and BSG) with the ACE2 gene was analyzed. The results showed that the ACE2 gene was expressed in all embryonic stages, except the morula stage. In the inner cell mass (ICM), although 80% of cells express ACE2, none of them express TMPRSS2; therefore, ICM is not susceptible to infection; however, in the epiblasts, many cells express both *TMPRSS2* and ACE2 genes together; consequently, they are likely to be infected at this stage [36]. Figure 2 shows the expression of genes in different stages of embryo development. Evidence shows that the human embryonic trophoblast is resistant to viral RNA and DNA and does not allow the virus to enter the follicle [37].

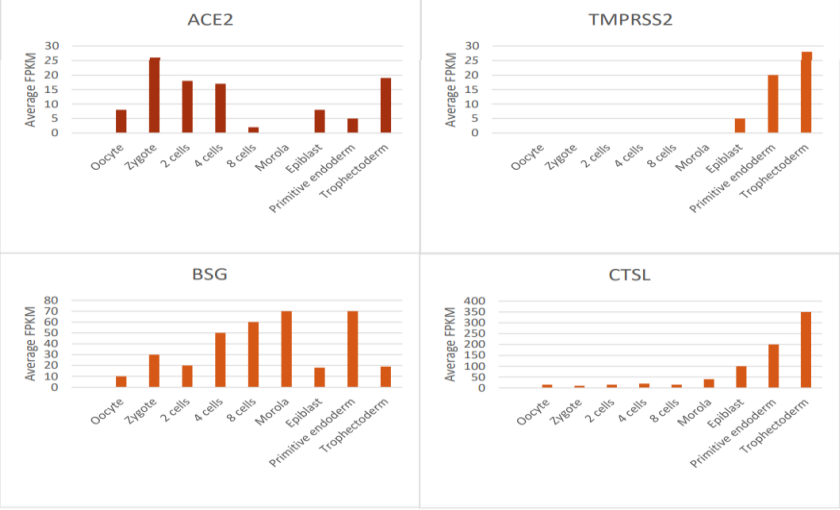

Figure 2. The mRNA expression of coronavirus receptors and spike proteins processing enzymes in the early human embryo development. Data were extracted from the single-cell RNA sequence of developing embryos. The X axis represents different stages of human embryonic development, and Y axis represents the fragments per kilobase of exon model per million reads mapped (FPKM) estimation [36].

The viral resistance is probably due to the high expression of the microRNA cluster, called C19MC in the trophoblasts. The C19MC expression is significant in the exosomes of primary human trophoblast (PHT) cells and the plasma of pregnant women [38]. Although there are no reports of an infected fetus in the uterus before birth, due to the presence of COVID-19 virus receptors in embryonic cells, it is necessary to inform couples about this issue during counseling before pregnancy. Also, if the infertility treatment cycle has been initiated, health protocols should be followed to protect the germ cells and the fetus. Couples can also freeze their gametes until the pandemic has been eradicated.

Although the presence of the new coronavirus in the fetus and placenta has not been reported, maternal exposure to the virus stimulates an inflammatory response in the fetus. This inflammatory response has been examined in the fetus by identifying interleukin-1 (IL-1), IL-6, IL-8, and tumor necrosis factor-α (TNF-α). The increase in these inflammatory markers and cytokines in the fetus can cause abnormalities of the central nervous system, vasodilation, and bleeding in animal models [39]. Also, these cytokines in humans can cause autism, schizophrenia, and psychosis [40].

5. Pregnancy

Evidence suggests that pregnant women are more prone to viral diseases than non-pregnant women. As previously reported, the susceptibility, incidence, and mortality of influenza virus in pregnant women are almost twice as high as non-pregnant women [41]. In Hong Kong, it has also been shown that death is 30% more common in pregnant women with SARS than non-pregnant women [42]. An increase in the level of progesterone increases the respiratory capacity by 50% through affecting the receptors in the hypothalamus; therefore, if there is a virus in the air, it can enter the respiratory tract of a pregnant woman [43]. An increase in progesterone level also increases the adhesion of the mucosal layer in the respiratory tract and increases the virus uptake [44].

The increased progesterone level in the first trimester leads to thymus degeneration and decreased CD4+ and CD8+ levels, resulting in poor immunity and increased vulnerability [45]. Physiological changes during pregnancy not only increase the risk of COVID-19 in pregnant women but also increase its severity. Also, cardiovascular changes during pregnancy increase metabolism and the need for oxygen, causing a 50-70% increase in shortness of breath in the third trimester, which can be exacerbated by COVID-

19 [46]. In pregnant women, the expression of ACE2 receptors in the placenta, uterus, and kidneys is doubled as compared to non-pregnant women [47]; this makes pregnant women more susceptible to the virus.

Also, mothers may not be able to differentiate the symptoms of COVID-19, such as shortness of breath, which is normal during pregnancy, and may visit clinics later than needed; this late referral can lead to the worsening of COVID-19 symptoms [48]. If pregnant women are diagnosed with COVID-19, prescription of medications can be a major challenge for physicians. Routine medications for COVID-19 (not definitive treatments) include hydroxychloroquine, metformin, lopinavir, methylprednisolone, and a type of glucosteroid that has been reported to be safe during pregnancy [49-51]. Glycoaestroids are not considered teratogenic during pregnancy, but their consumption may cause high blood pressure, diabetes, weight gain, premature membrane rupture, and restriction of intrauterine growth. Therefore, caution should be exercised in prescribing this group of drugs [48].

Interferon therapy is one of the safe antiviral therapies during pregnancy, which is effective in the treatment of hepatitis C virus in pregnant women, with no serious side effects reported so far [52]. Also, plasma injections for pregnant women with the disease can alleviate the symptoms. Of course, as usual, blood grouping (ABO) should be considered [53]. Also, favipiravir, ribavirin, and tocilizumab have been shown to have teratogenic effects during pregnancy and should not be prescribed during pregnancy. Although no study has yet reported the birth of an infected newborn, it has been proven that a newborn may be infected with a virus after birth in the hospital setting [54-57]. Moreover, diagnostic surgery should be prescribed with more caution for mothers who have COVID-19 symptoms. For example, if amniotic fluid surgery or fetoscopy is needed, it is suggested to replace it with the chorionic villus sampling (CVS) method, which decreases the possibility of transmission [58].

6. Vertical transmission

So far, no newborn has been tested positive in throat and blood tests at birth. The RT-PCR assay of nine women with COVID-19 showed no viral RNA in the amniotic fluid, umbilical cord, milk, or vaginal specimens. However, in rectal samples, coronavirus RNA was confirmed in ten infected women. The presence of the virus in the stool suggests that natural childbirth should not be prescribed to infected mothers [59]. An increase in IgG and IgM was reported in a neonate born to an infected mother [60]. An increase in IgG may be attributed to the mother's immune response to the virus and the transmission of the antibody from the mother to the fetus through the placenta. Nevertheless, since IgM cannot cross the placenta, its increase in the fetus indicates fetal infection in the mother's uterus, followed by immunity. ACE2 is also expressed in the placenta, but its expression is very low in the syncytiotrophoblast (STB) cells, decidual stromal cells, and placental epithelial cells [61].

7. Birth

As mentioned earlier, no viral RNA has been found in the amniotic fluid or vaginal specimens of COVID-19 patients. However, the virus was found in the mothers' rectal samples. Therefore, the passage of the newborn through the birth canal alone cannot cause COVID-19. The associated complications during pregnancy can lead to high-risk labor. Almost all cases of severe maternal infection cause preterm delivery and cesarean section. Cesarean section was reported to reduce the risk of neonatal infection. However, it has some disadvantages and can reduce the antibody expression in the fetus due to the lack of passage through the birth canal, and therefore, the lack of immunity to other infections [48].

8. Freezing of sperms, oocytes, and the umbilical cord blood

Although CDC has not yet confirmed the presence of live and pathogenic COVID-19 viruses in non-respiratory fluids, such as vomit, urine, milk, and semen, the Society for Assisted Reproductive Technology (SART 2020) suggested that individuals with a definite diagnosis of COVID-19 avoid fertilization [62], as there are reports of very low titers of the virus in non-respiratory fluids [63]. Overall, the possible presence of the virus in the semen is a reason to refrain from freezing the sperms of infected or suspected individuals. These viruses are known to survive at very low temperatures. For example, the flu virus can stay alive and pathogenic for up to 40 years. Also, coronaviruses, similar to the influenza virus,

contain RNAs and envelopes; therefore, the virus may survive in freezing conditions for a long time [64]. In China, the umbilical cord mesenchymal stem cells were found to be effective in treating patients with the acute symptoms of COVID-19. Physicians at the Italian College of Anesthesia were also able to reduce the number of patients admitted to the ICU, using the umbilical cord mesenchymal stem cells [65].

9. Infertility treatment

Male infertility occurs in 15% of all men and 50% of all infertility cases [66]. It is recommended that during the current pandemic, couples avoid going to clinics for infertility treatment. They can communicate virtually with their physician and identify the possible causes of infertility by providing their history. Semen samples can also be sent to the physician in charge, followed by the hormonal profile and relevant genetic tests. However, if couples insist on starting their treatment or freezing their gametes for emergency or personal reasons, they can start their treatment. Also, couples should be interviewed before visiting their physician so that they can attend the clinics if they do not have the initial symptoms [67]. These couples need to be given special counseling for the COVID-19 pandemic, based on the existing problems in the first visit until pregnancy checkups and finally birth so that they can make a logical decision.

On March 19, 2020, the ESHRE recommended that all infertile patients, who have started their treatment cycle, refrain from pregnancy, and freeze their gametes until the conditions are normal again. However, this suggestion was made for reducing the burden of COVID-19 on the healthcare system and hospitals [68]. In the United Kingdom, the HFEA released its guidelines on March 18, calling for a halt to reproductive therapies in the coming weeks to minimize the spread of the virus and reduce the possible impacts on the healthcare system [69]. Moreover, on March 17, the FSA declared that there are not enough reasons or resources to recommend against pregnancy during the pandemic, neither naturally nor medically. However, on March 24, with an increase in the epidemics in Australia and New Zealand, this group recommended that non-emergency pregnancies be avoided to preserve resources, including the personnel and equipment, for the treatment of patients with COVID-19 who require hospital care [70].

Discussion

Today, the number of casualties and new cases of infection with the new coronavirus has become a major global concern. In addition to its common problems and symptoms, the virus can also damage the internal organs. In this study, we aimed to analyze the damages of COVID-19 on the reproductive system, fetus, pregnancy, and vertical transmission, as half of infected cases are of childbearing age [19]. According to our findings, men are more likely to develop the disease than women due to hormonal factors; however, pregnant women are more vulnerable to the virus. One of the reasons for this vulnerability may be the increased level of progesterone [44]. According to the review of various studies on the effect of COVID-19 on male fertility, although the presence of this virus has not been confirmed in the semen yet, due to the presence of ACE2 receptors in different parts of the male reproductive system, it is not unexpected to find the virus in the male reproductive system of new cases. There are also studies showing that the virus can cause some damages to the testicular tissue, such as orchitis [17].

According to our observations, the new coronavirus may also enter the female reproductive system and cause damages. The COVID-19 virus may attack the ovarian tissue, granulosa cells, and epithelial tissue of the endometrium [23]. The result of this attack can be a decrease in implantation, and ultimately, a decrease in female fertility. By comparing the effects of coronavirus on the male and female reproductive systems, we concluded that due to the presence of more receptors in the male reproductive system than females, damage to the female reproductive system is more destructive. This may be due to the fact that a woman's ovarian reserve remains unchanged throughout her life and is prone to various damages, while a new sperm is produced in the man's body during spermatogenesis, and the risk is greatly reduced.

The impact of the virus on the fetus is lower than its impact on mothers, because trophoblasts are largely resistant to the entry of the virus, and the embryo can be considered naturally resistant to infection at the time of embryo formation in the

uterus. However, in later stages of pregnancy, in addition to the possibility of uterine contamination due to maternal infection, there is also the possibility of inflammation affecting the fetus, causing serious damage to the fetus. To reduce the potential risks, obstetricians and gynecologists are recommended to use cesarean section instead of natural childbirth (cesarean section was reported to reduce the risk of infection in newborns) or use less invasive methods, such as CVS, if fetal surgery is needed [48, 58].

Although the possibility of vertical transmission from the mother to the fetus in late pregnancy has been rarely reported, it is possible that the COVID-19 virus alter the expression of ACE2 in the uterus in early pregnancy. The presence of IgM in the fetal blood is a warning sign that the fetus is possibly infected with the virus, and the newborn, especially if there is a history of lung or heart disease, is more likely to die from the coronavirus [60,61]. Moreover, infection through vertical transmission may occur after giving birth as a result of maternal care of the neonate and the lack of distance between them. By comparing the risk in different stages, it can be concluded that the greatest risk to newborns in different stages of fertility occurs at birth because the fetus is protected by trophoblasts in the early stages, while later in pregnancy, the probability of passing the virus through the umbilical cord is very low [59].

During the COVID-19 pandemic, infertility treatment is not considered a health emergency. It is also not recommended for couples to consider pregnancy because even if the infertility problem is resolved, the couple will face a high-risk pregnancy. However, in many countries, infertility treatment is not prohibited, and couples can visit fertility treatment clinics. Therefore, the medical staff must acquaint the couples with the possible risks so that they can decide according to their circumstances. However, infertility treatment is an emergency for cancer patients who are planning to start chemotherapy or women who are approaching menopause and want to become pregnant after the pandemic. Therefore, these patients and those who started their infertility treatment program before the pandemic can cryopreserve their gametes or zygotes. Pregnant mothers are also advised to store the umbilical cords in the umbilical cord banks because if the mother or the child is affected by COVID-19, the umbilical cord can have therapeutic effects or may even compensate for the possible COVID-19 damage to the tissues, including the lungs, and cause liver damage after recovery [65]. It is also suggested that cryopreservation centers use separate tanks during the outbreak so that the samples of previous years are not contaminated.

It is important that non-pregnant women and those who do not intend to become pregnant adhere to the WHO recommendations for COVID-19, similar to men. Also, women who are pregnant or are planning to become pregnant should follow the instructions strictly. Asymptomatic carriers are a major problem in the spread of the disease, as they can infect their spouses without knowing it. Therefore, it is recommended that infected men and possible carriers (e.g., travelers to high-risk cities or those who have been in direct contact with patients) abstain from sex for at least two weeks. Also, in fertilization laboratories, embryologists should be careful while working with oocyte and sperm samples and follow all hygienic principles.

Conclusion

The presence of the new coronavirus in the male and female reproductive systems has not been confirmed yet. However, the presence of virus receptors in these organs, besides case reports from around the world, suggests that the virus may enter the reproductive system. The presence of the virus in the male and female reproductive tracts not only may harm themselves but also can endanger the health of the next generation. Therefore, couples are advised to avoid pregnancy during this pandemic. During the pandemic, couples are more susceptible to the infection during pregnancy (from fertilization until childbirth). Also, the coronavirus receptors in the embryo and fetus allow the virus to attack and threaten the health of the fetus. Even if COVID-19 itself does not cause abnormalities in the reproductive system, its complications, such as fever and shortness of breath, can cause problems for both the mother and the fetus. People who have started their infertility treatment cycle are also advised to freeze their gametes and wait until the pandemic is over. Overall, pregnant

women must strictly adhere to the WHO health guidelines to be less exposed to the virus.

One of the limitations of this study is that the articles and data related to COVID-19 are increasing every day; therefore, some new data may be published in scientific databases after writing this article. Since little is known about the new coronavirus, there is a special need for case reports by physicians and research by scholars to provide a more realistic view of this disease for the public.

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Conflict of interest

There is no conflict of interest.

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