

# COVID-19 in Seminal Fluid

Subjects: **Infectious Diseases**

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Major concerns about the impact of SARS-CoV-2 infection on male fertility have increased, and one of the important questions is the present probability of COVID-19 in the seminal fluid of infected individuals. For the detection of virus co-expression, both angiotensin I-converting enzyme 2 (ACE2) and transmembrane serine protease TMPRSS2 were required in the testis of COVID-19 individuals, raising concerns regarding the virus entrance from the blood–testis barrier and the presence of COVID-19 in testis tissue and seminal fluid.

infertility

COVID-19

sperm

SARS

vaccine

## 1. Sperm Count

Recently, Hu et al. assessed the effects of COVID-19 infection on sperm quality in recovered patients compared to healthy cases <sup>[1]</sup>. The results of their study showed that COVID-19 can significantly decrease sperm count in comparison with the control group. It is also reported that sperm count in recovered patients' after 150 days was similar to the control group. So, at least 5 months recovery time is needed for sperm count to return to normal. Finally, they concluded that the recovery time in COVID-19 patients plays an important role in increasing sperm quality, especially sperm count. Therefore, COVID-19-infected patients after treatment must receive supplemental care to improve sperm count. In another study, the seminal samples of COVID-19-infected patients after recovery were analyzed and compared with healthy men. The results revealed that sperm count was significantly lower in recovered patients than in the control group <sup>[2]</sup>. Segars et al. demonstrated that the fertility potential is decreased in COVID-19-infected patients and sperm analysis showed reduced sperm count 3 months post COVID-19 infection <sup>[3]</sup>. Holtmann et al. in their study, evaluated the effects of COVID-19 on sperm parameters, demonstrating that in COVID-19-infected patients, sperm concentration is significantly decreased <sup>[4]</sup>. In a study published in 2022, sperm count was assessed in COVID-19-recovered patients and there was a significantly decreased sperm count in patients 1 month post recovery in comparison with 3 months, revealing that recovery time is an important factor for sperm count improvement post COVID-19 infection <sup>[5]</sup>.

Guo et al. in 2021 confirmed that sperm count was significantly decreased in COVID-19-infected patients, suggesting that a direct effect of COVID-19 on spermatogenesis may be responsible for sperm count decrease in COVID-19 patients <sup>[6]</sup>. A study by Li et al. reported that sperm count was decreased in COVID-19 cases, suggesting that elevation of immunological factors, including interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF-

α), might be responsible for differences in sperm count between COVID-19-infected patients and healthy control individuals [7]. Additionally, another study concluded that the elevation of sperm DNA fragmentation is likely the cause of sperm count decrease in COVID-19-infected patients [8].

## **I 2. Sperm Motility**

Several studies investigated the effects of COVID-19 infection on sperm motility and reported decreased sperm motility in patients compared to healthy individuals [3].

Assessing sperm parameters in COVID-19-infected men, Piroozmanesh et al. demonstrated that sperm motility was significantly decreased [9]. Holtman et al. in their study, confirmed a sperm motility decrease in COVID-19 moderately infected patients [4]. Similarly, Li et al. reported that SARS-CoV2 infection can have negative effects on sperm mobility in fertile infected individuals [7]. Recently, Donders et al. reported significantly decreased sperm motility immediately after COVID-19, which was reversed and finally increased 3 months post infection compared to 1 month [5].

Interestingly, in contrast to the above-mentioned papers, Guo et al. analyzed the sperm quality of COVID-19-infected patients and reported that among 23 patients, only in 2 cases was the sperm motility decreased, revealing that in their study population COVID-19 had no negative effect on sperm motility [6]. He et al. in 2021 established that sperm motility was influenced by infection. They reported that sperm motility was significantly decreased during moderate infection in comparison with mild infection or healthy control individuals [10]. The elevation of oxidative stress and damage to sperm DNA are other factors for decreased sperm motility in viral infection cases [11].

## **I 3. Sperm Morphology**

Sperm morphology is a vital parameter in the sperm analysis process. Sperm morphology, concerning the size and shape of sperm, is one factor that is examined as part of a semen analysis to evaluate male infertility. Changes in sperm shape may have negative effect on sperm motility, viability and fertility potential. Several factors can generate defects in sperm morphology. Infection is one of these factors. After the COVID-19 pandemic, an important question about whether COVID-19 is a defective factor for sperm morphology has arisen. A recent study investigated the effects of COVID-19 on sperm morphology in three groups, namely infected patients before and after treatment and healthy control males. In the infected patients before treatment, sperm morphology was significantly decreased in comparison with the control group. Furthermore, in treated individuals, sperm morphology was impaired compared to the control group. They concluded that a continuous fever during COVID-19 was an aggravating factor for sperm morphology [12]. A study by Ma et al. demonstrated that the normal morphology of sperm in COVID-19 patients is significantly decreased [8]. In 2021, Falahieh et al. assessed sperm morphology in treated COVID-19 cases after 3 months. The results of their study showed that the percentage of normal sperm morphology increased 3 months after COVID-19 treatment, but based on WHO guidelines, the rate

of normal morphology was lower than standard [13]. Maleki et al. showed that sperm morphology can be decreased after SARS-CoV2 infection [14]. Koc and his colleagues [15] investigated sperm parameters of 21 infertile men who were referred for infertility treatment. The results of COVID-19 tests in these cases were positive without requiring hospitalization. This study showed that normal sperm morphology was significantly decreased.

Since COVID-19 can activate several pathways throughout inflammatory responses, it can induce further oxidative stress. This oxidative stress can cause peroxidative impairment to the plasma membrane of sperm. This process can create defects in sperm chromatin and DNA integrity, which leads to abnormal sperm morphology [16]. On the other hand, fever associated with infection constitutes a defective factor for sperm morphology. Other researchers suggested that the level of fever (mild/medium/severe) and its duration (number of days) are two main parameters that can significantly decrease normal sperm morphology parameters [11]. Two separate studies confirmed that high fever levels demonstrated a negative correlation with normal sperm morphology [17][18]. It is speculated that the decrease in normal sperm morphology during COVID-19 can be attributed to fever levels.

## 4. Sperm Viability

Sperm viability in COVID-19 infection was investigated in some studies. The results of studies confirmed that sperm viability was decreased in COVID-19 patients [2]. Falahieh et al. assessed sperm analysis of 20 COVID-19 patients 2 weeks and 3 months post infection. They found that sperm viability had no significant difference between two investigation time frames [13]. However, Piroozmanesh and his colleagues compared sperm viability in infected patients and healthy control men, showing that sperm viability was significantly decreased in COVID-19 patients [9].

Several mechanisms have been proposed for the negative effects of COVID-19 on sperm viability. Firstly, there is a hypothesis that influenza SARS-CoV-2 viruses cause oxidative stress that negatively affects sperm viability [19]. Secondly, elevation in inflammatory factors, including cytokines, TNF- $\alpha$ , and interleukin-2, 6, can induce lipid peroxidation in sperm, leading to sperm viability damage [20]. Marin et al. have suggested that COVID-19 can induce ACE2 production, and this is a negative factor for sperm viability in COVID-19 patients [21]. Based on Kopper's study, COVID-19 may induce apoptosis and lead to sperm viability impairment [22].

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