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Effect of COVID-19 (SARS-CoV-2) on Male Fertility: A Systematic Review

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ABSTRACT

Background: *The COVID-19 pandemic, caused by SARS-CoV-2, it has effect on multiple organ systems, including the male reproductive tract, necessitates a comprehensive assessment of its effects on fertility parameters.* ***Methods****: This systematic review synthesis evidence from meta-analysis, clinical studies and autopsy reports examining the effect of COVID-19 on male fertility. Studies investigating sperm parameters (volume, concentration, motility, morphology), viral presence in semen, reproductive hormone levels and testicular histopathology in COVID-19 patients and recovered individuals were analyzed.* ***Results:*** *COVID-19 infection significantly impairs sperm parameters, with meta-analysis demonstrating reductions in sperm count, total motility notably progressive motility and morphology. detection of SARS-CoV-2 in semen remain rare (approximately 3-8% of cases) mostly during the acute phase. Hormonal alterations involve reduced testosterone levels and elevated luteinizing hormone, suggesting primary testicular damage and hypothalamic -pituitary gonadal axis dysfunction, Autopsy studies showed orchitis, inflammatory infiltrates, Leydig cell damage, spermatogenesis impairment, blood-testis barrier compromise. Most alterations show partial recovery within 3-6 months post-infection, though some patients exhibit persistent abnormalities.* ***Conclusion****: SARS-CoV-2 infection negatively affects male fertility through multiple mechanisms including direct viral invasion, inflammatory responses, hormonal dysregulation and fever induced damage. While several parameters recover over time, long-term monitoring of reproductive function in recovered patients is warranted. Further research is needed to interpret the full extent of COVID-19s effect on male fertility and to develop targeted interventions.*

Keywords: COVID-19, SARS-CoV-2, Males Fertility, Sperm Parameters, Testicular Histopathology, Orchitis, Reproductive Sex Hormones, Spermatogenesis, Seminal Fluid.

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INTRODUCTION

Infertility is reproductive systems disorders (R. Li et al., 2022; Siahpoosh et al., 2021) which about 20% of reproductive aged couples suffer from infertility (Farsimadan, Haje, et al., 2021; Farsimadan, Moammadzadeh Ghosi, et al., 2021). Male factors constitute 40-50% from infertility cases (Farsimadan & Motamedifar, 2020) . Pathological agents particularly viruses, play an important role in infertility (Farsimadan, Riahi, et al., 2021; Farsimadan & Motamedifar, 2021). Viruses are a major cause of fertility problems through the ability to influence male reproductive function (Hezavehei et al., 2021).

The coronavirus disease 2019 (COVID -19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has emerged as one of the most important global crises of the 21 st century. Since its initial detection in Wuhan, China. in December 2019, the virus has infected hundreds and millions of individuals worldwide resulting in substantial morbidity and mortality (Umesh et al., 2022). This new viral strain led to life threatening complications include fever, nasal congestion, asthenia, anosmia, ageusia and dyspnea in human and has shown to spread quickly (Farsimadan & Motamedifar, 2023). COVID-19 is primarily characterized respiratory manifestations accumulating evidence indicates the SARS-CoV-2 is multi-organ pathogen capable of affecting various physiological system, including the cardiovascular, gastrointestinal, neurological and reproductive system (Teixeira et al., 2021). Both humans' genders

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are vulnerable to COVID-19 infection, infection rates in men higher than women (Jin et al., 2020). Male reproductive system has emerged as a potential SARS-CoV-2 infections due to high expression of angiotensin -converting enzyme 2(ACE2) receptors and transmembrane serine protease (TMPRSS2) in testicular tissues (Luddi et al., 2022; Massarotti et al., 2021). ACE2 serves as the primary cellular entry receptors to SARS-CoV-2, it is high expression in spermatogonia, Leydig cell, Sertoli cells and seminiferous tubules suggest that the male reproductive system may be vulnerable to viral invasion (Giugliano et al., 2025; Moshrefi et al., 2021). This vulnerability raises critical concerns about potential impact of COVID-19 on male fertility, particularly given that a significant proportion of infected individual are of reproductive age.

Multiple mechanisms have been proposed to explain how SARS-CoV-2 might impact male reproductive function. These include direct viral invasion of testicular cells, systemic and local inflammatory responses (cytokine storm), fever-induced thermal stress on spermatogenesis, disruption of the blood-testis barrier (BTB), hormonal dysregulation through hypothalamic-pituitary gonadal (HPG) axis dysfunction, and oxidative stress (Akhigbe et al., 2022; Peirouvi et al., 2021; Zadeh et al., 2021). The potential for both acute and long-term reproductive consequences have prompted extensive investigation into the impact of COVID-19 on semen parameters, hormone levels, and testicular histology.

Early reports of orchitis and scrotal discomfort in COVID-19 patients, coupled with autopsy findings showing testicular pathology, have massive concerns about fertility implications (Mikhail et al., 2021; Yao et al., 2021). On the other hand, studies testing semen quality in recovering patients have yielded variable finding, with some reporting significant impairments and others finding minimal or transient effects (Aksak et al., 2022; Edimiris et al., 2023). This variance in findings may reflect differences in timing of evaluation post-infection, disease severity, methodological approaches and patients' demographics.

The rational of this systematic review stems from the need to synthesize the rapidly expanding body of literature on COVID-19 and male fertility. Perception the full spectrum of reproductive effects is essential for several reasons first: to provide clinical advice of male patients of reproductive age who have recovered from COVID-19, second; to guide recommendations regarding preservation. third: to distinguish patients who may require long-term andrological follow-up; fourth; to explanation the underling pathophysiological mechanisms of male reproductive system dysfunction resulting from COVID-19 infection. This review comprehensively investigates the effect of COVID-19 infection on sperm parameters, viral presence in semen, reproductive male hormone profile and testicular histopathology, providing an evidence-based assessment of the current state of knowledge in this critical area of reproductive medicine.

METHOD

Search Strategy

A systematic literature search was conducted across PubMed/MEDLINE, Scopus, Web of Science and Google Scholar to identify relevant studies published from January 2020 to August 2026. The search combined MeSH (Medical Subject Headings) and Key words involved: ''COVID-19'', ''SARS-CoV-2'',''male fertility'', ''Semen parameters'', ''sperm motility'', ''sperm morphology'', ''sperm count", seminal fluid ", testosterone ", "FSH", "LH", "orchitis", "testicular histology ", and "spermatogenesis". Reasonable operators (AND/OR) were used to refine the search.

Eligibility Criteria

Studies were included if they :(1) record male patients with confirmed COVID-19 diagnosis by serological testing or RT-PCR); (2) reported at least one outcome related to sperm parameters, viral detection in semen, male reproductive hormonal levels or testicular histopathology; and (3) were published in peer-reviewed journals with a retrievable digital object identifier (DOI). A total of 78 studies were included in this review from different countries, study designs were heterogenous, eligible study designs encompassed randomized and non-randomized controlled studies, prospective and retrospective cohort studies, meta-analysis, case -control studies, systematic reviews, cross-sectional analysis and autopsy -based reports. Sample size ranged from small pilot studies to large multicenter cohorts. Disease severity varied across studies, ranging from mild, moderate and severe

COVID-19, with several studies also testing patients in the post-recovery phase at intervals ranging from one to twelve months post-infection. Exclusion criteria were: non-human studies, studies without a confirmed COVID-19 diagnosis, conference abstracts without full-text data and duplicate publications reporting the same dataset.

Study Selection and Data Extraction

Records retrieved from all databases were incorporated and de-duplicated, titles and abstracts were checked against the eligibility criteria. The following data were extracted from each included study: first author and year, country, sample size, study design, age pf participants COVID-19 severity, outcome measures reported (semen parameters, seminal viral detection, male hormones levels, histological outcomes), timing of assessment relative to infection and key findings. Data were organized thematically according to the review's main subjects.

Effect Of Covid-19 On Sperm Parameters

The effect of COVID-19 infection on semen quality has been extensively investigated through prospective cohort studies, retrospective analyses, and meta-analyses. Semen analysis remains the cornerstone of male fertility assessment, with parameters including volume, concentration, motility, and morphology serving as key indicators of reproductive potential. Emerging evidence suggests that COVID-19 can adversely affect multiple sperm parameters, though the magnitude and duration of these effects remain subjects of ongoing investigation.

Semen Volume

Semen volume reflects the secretory function of seminal and prostate gland, has shown variable response to COVID-19 infection across several studies, meta-analysis by (Xie et al., 2022) showed that the SARS-CoV-2 infection negatively effect on seminal volume with standardized mean difference of -0.27 (p=0.00), indicate statically significant difference reduction compared to control groups.

The findings of another study (Koc & Keseroğlu, 2021) confirmed significant reduction in semen volume following COVID-19 infection, with median value decreasing from 3.0 mL to 2.5 mL (p=0.005) in a cohort of 21 infertile men. According to meta-analysis from previous investigations (Erbay et al., 2021; T. H. Guo et al., 2021) that subjects recovered from COVID-19 have semen volume about 0.2 ml less than un-affected males (overall MD − 0.20; 95% CI − 0.45, 0.05). Kariyev et al., (2025) concluded that the ejaculate volume was reduced by half in men who recovered from COVID -19 compared to those without infection history. However, not all studies have demonstrated significant volume changes. ElSaeed & Emam (2024) found no statistically significant change in semen volume at 3- and 6-months post-infection in a prospective study of 44 reproductive-aged men. Likewise, Pazir et al. (2021) reported no significant difference in semen volume (p=0.56) in 24 men who recovered from mild COVID-19, with samples collected at a median interval of 111.5 days post-infection.

The inconsistency in semen volume findings it could be the results of a difference of disease severity, individual patient's factors and timing of evaluation, The accessory glands contributing to semen volume express ACE2 receptors, suggesting potential for direct viral effects, though fever and inflammation may play more constant role in volume changes (Ismail, 2023).

Sperm Count (Concentration)

Sperm concentration is one of the most important affected parameters following COVID-19 infection. Several studies have significant reduction in sperm count and concentration in recovered patients. Xie et al. (2022) reported in their meta-analysis that the SARS- CoV -2 negatively affected sperm concentration (SMD = -0.41, p=0.002) and sperm count (SMD = -0.30, p=0.00). These finding suggest substantial impact on spermatogenic function.

Hu et al. (2022) investigated the role of virus infection on semen parameters in recovered patients relative to health control. Their finding demonstrated that COVID-19 infection was associated with a significant reduction in sperm count compared to the control group. Notably, sperm count in recovered patients returned to levels comparable to those of healthy controls after approximately 150 days, indicating that minimum recovery period of five months is required for spermatogenetic function to normalize. The authors concluded that the duration of post-infection recovery is a critical determinant in the restoration of sperm quality, particularly with respect to sperm count. Consistently with these findings, Ruan et al. (2021) conducted a comparative analysis of seminal parameters in COVID-19 recovered males versus healthy individuals, and similarly reported a significantly lower sperm count

among recovered patients relative to the control group.

Guo et al. (2021) showed a significant decline in sperm count among COVID-19 patients, suggesting a direct adverse effect of the virus on spermatogenesis as a plausible mechanism underlying the observed reduction. consistent with these finding, Li et al. (2020) similarly reported decreased sperm count in COVID-19 cases, proposing the elevation of pro-inflammatory mediators-specifically interleukin-6 (IL-6) and tumor necrosis factor- a (TNF- a)- may account for the marked differences in sperm count observed between COVID-19 patients and control group. Dipankar et al. (2022) revealed that sperm count was 46.45 million/ejaculate during COVID-19, significantly lower than normal value ($p<0.05$), but enhanced to 161.6 million/ejaculate after 74 days ($p=0.000$). The temporal pattern of concentration changes suggests the spermatogenic process deterioration occurs during or shortly after infection, with gradual recovery over subsequent months. The approximately 74-days spermatogenic cycle explain why improvement are typically observed 2-3 months post infection (Chun-Ling et al., 2024).

Total Sperm Motility

Total sperm motility includes in both progressive and non-progressive movement, has emerged as one of the most significantly impaired parameters following COVID-19 infection. Koc & Keseroğlu, (2021) noted significant decreases in total motility after COVID-19, with values declining from 48.6±22.1% to 34.7±20.7% ($p=0.001$). Pazir et al. (2021) found that total motility decreased significantly after SARS-CoV-2 infection ($p=0.01$) compared to pre-infection values, despite finding no significant changes in volume or concentration.

Multiple studies have examined the effect of COVID-19 infection on sperm motility, consistently reporting a significant reduction in motility amount infected patient's relatives to healthy individuals. In an assessment of semen parameters in infected men, Piroozmanesh et al. (2021) showed a statically significant impairment od sperm motility. Similarly, Holtmann et al. (2020) corroborated these findings, confirming a notable decline in sperm motility in patients with moderate COVID-19 infection.

He et al. (2021) further demonstrated that the motility of sperms was adversely affected by infection severity, reporting a significantly greater reduction in motility in patients with moderate infection compared to those with mild infection of healthy group. Beyond the direct viral effects, oxidative stress and sperm DNA damage have been identified as additional contributing mechanisms underlying the decline in sperm motility observed in the context of viral infection (Carlsen et al., 2003).

The mechanisms underlying motility impairment likely involve multiple factors, including oxidative stress, inflammatory cytokines, mitochondrial dysfunction, and structural damage to the sperm flagellum (Bani et al., 2022). The observation that motility often shows more pronounced impairment than concentration suggests that COVID-19 may affect sperm function even when spermatogenesis is relatively preserved.

Progressive Motility

Progressive motility, defined as sperm moving actively in a straight line or large circles, is particularly critical for fertility as it reflects the sperm's ability to traverse the female reproductive tract and penetrate the oocyte. COVID-19 has been shown to significantly impair progressive motility across multiple studies. Xie et al. (2022) reported that progressive motility was negatively affected by SARS-CoV-2 infection (SMD = -0.35, $p=0.01$).

Koc & Keseroğlu (2021) found significant decreases in progressive motility after COVID-19, with values declining from 35.1±21.7% to 21.8±15.9% ($p<0.001$). Wang et al. (2025) reported that progressive motility was significantly reduced during the peak-outbreak period (37.7% vs. 45.1%, $p<0.001$) compared to pre-outbreak levels, returning to baseline in the post-outbreak period. Chun-Chun-Ling et al. (2024) found that progressive motility was significantly lower 30-71 days postinfection (39.76% vs. 46.88%, $p=0.0243$) compared to pre-infection levels, but by 77-125 days post-recovery, progressive motility improved and showed no significant differences from preinfectional levels. Another study (Zhang et al., 2025) demonstrated that progressive motility significantly decreased in the first month post-COVID-19 and negatively correlated with body temperature above 38°C, with alterations reversing by the third month. The preferential impairment of progressive motility over total motility suggests that COVID-19 may affect the energy metabolism and structural integrity of sperm, particularly the axonemal components responsible for directional movement (Ghazavi et al., 2025).

Sperm Morphology

Sperm morphology is a vital parameter for semen analysis to evaluate male infertility, it reflects the structural integrity of the sperm head, midpiece, and tail. The changes in shape might have adverse effect on the motility and viability and fertility potential. There are many parameters can cause defects in the morphology of the sperm, one of these is infection. After the pandemic, an essential question has arisen whether COVID-19 is a defective factor for sperm morphology or not. According the investigation by Koc & Keseroğlu (2021) revealed a significant decrease in normally shaped sperm after COVID-19 infection, with median value reducing from 6% to 5% (p=0.015). A study by ElSaeed & Emam (2024) found the normal morphology is significantly declined at both 3 and 6 months after infection compared to baseline, with partial recovery at 6 months.

In 2025, Kariyev et al. (2025) observed the percentage of abnormal sperm forms was twice as high in males who recovered from COVID-19 compared to those without any infection history. Chun-Ling et al. (2024) revealed that the normal sperm morphology was significantly lower 30-71 day after infection (2.70% vs 3.58% p=0.0299) compared to pre-infection levels, but within 77–125-day post recovery the sperm morphology improved and showed no significant difference from pre-infection levels. Another study (Majidipour et al., 2025) concluded presence significant difference in normal morphology (p=0.001) between COVID positive and COVID negative groups. Zhang et al. (2025) observed that the percentage normal sperm morphology significantly reduced in first month post COVID-19 infection, with alteration reversing by third month.

The impact of COVID-19 infection on morphology is due to DNA damage caused by oxidative stress, disturbance of spermatogenesis (the final maturation phase of sperm development), and inflammatory effects on testicular microenvironment (Araújo et al., 2024). It is should be noted that the sperm morphology often shows slower recovery compared than other parameters suggests that structural damage may require more time to resolve or may reflect damage to earlier stages of spermatogenesis.

Presence of SARS-CoV-2 in Seminal Fluid

The existence of SARS-CoV-2 in seminal fluid has been a subject of intense investigation due to it is implications for sexual transmission and directs viral effects on the male reproductive system. The presence of angiotensin –converting enzyme 2 receptor in testicular tissues, especially in spermatogonia, Leydig cells, and Sertoli cells, this suggests that the virus likely infects the male reproductive tract (Giugliano et al., 2025; Luddi et al., 2022). However, the actual detection rate of viral RNA in semen have been relatively low and variable across studies.

A study confirmed that SARS-CoV-2 RNA was detected in 6 out of 38 semen sample of COVID-19 patients, with 4 in acute phase and 2 recovering patients, although four other studies found no viral RNA in semen or prostate discharge (Trypsteen et al., 2020).

Another study by Corona et al. (2022) conducted a systematic review and meta-analysis reporting the actual detection rate 8% (5-12%) for SARS-CoV-2 m RNA in seminal fluid, the detection rate is high significantly when sample were collected less than 11 days after diagnosis. In 2021, Saylam et al. (2021) detected SARs-CoV-2 in four (13.3%) patients semen sample taken the day after positive pharyngeal and/or nose swab, with detection associated with sever clinical condition and high very viral load.

Conversely to the above studies, numerous studies confirmed that there was no COVID-19 virus detection in semen for infected individuals. For example, the study by (Kayaaslan et al., 2020) tested SARS-CoV-2 RNA in semen sample of 16-acute phase of COVID-19 patients by using RT-q PCR, with all sample being negative for SARS-CoV-PCR. Pavone et al. (2020) found no SARS-CoV-2 RNA in semen of nine Italian patients recovering from mild COVID-19 infection, and samples were collected within 13 days of their last positive nasopharyngeal swab.

The inconsistency between high ACE-2 expression in testicular test and low probability detection the virus in seminal fluid may be interpret by many factors. First, the blood -testis barrier (BTB) may supply protection against viral entrance under the most circumstance, with breach occurring only in severe cases or when systematic inflammation is pronounced (Paoli et al., 2021).

Second the timing of sample collation is critical, as viral shedding in semen appear to transient and primarily occur during the acute phase of infection (Corona et al., 2022). Third, the sensitivity and specificity methods that used to detect the virus may vary, and some studies have employed more sensitive techniques as digital droplet PCR (Luddi et al., 2022). The implications of these findings are significant for clinical practice. The low detection rate of SARS-CoV-2 in semen suggest that the sexual transition is unlikely, notably post the acute phase of infection (Verrienti et al., 2022).

Effects of COVID-19 on Male Reproductive Sex Hormones

The hypothalamic -pituitary -gonadal (HPG)axis plays a central role in regulating male reproductive function, with testosterone serving as the primary male sex hormone essential for spermatogenesis, secondary sexual characteristics and sexual desire. COVID-19 has been shown to significantly impairment this hormonal axis, with implications for both acute illness and long- term reproductive health.

Testosterone Hormone

Testosterone levels have been consistently reported to be reduced in COVID-19 patients across several studies. Cinislioglu et al. (2022) found that serum total testosterone (TT) levels in COVID-19 patients were significantly lower (median 140 ng/dL) compared to controls (median 322 ng/dL, $p<0.001$), with severe COVID-19 patients having significantly lower TT (median 85.1 ng/dL) than mild-moderate patients (median 315 ng/dL, $p<0.001$). Patients needing intensive care had lower TT (median 64.0 ng/dL) versus those not needing it (median 286 ng/dL, $p<0.001$), and non-survivors had lower TT (median 82.9 ng/dL) versus survivors (median 166 ng/dL, $p<0.001$).

Koc & Keseroğlu (2021) observed a significant decline in testosterone levels after COVID-19 diagnosis, decreasing from 350.1±115.5 ng/dL to 289.8±103.3 ng/dL ($p=0.009$). Lan et al. (2024) conducted a meta-analysis showing that COVID-19 significantly decreased testosterone by 3.94nmol/L ($p=0.0007$) and the testosterone to luteinizing hormone (T: LH) ratio by 0.39 ($p=0.04$). Albayaty et al. (2024) observed that serum testosterone levels were significantly lower in COVID-19 recovered patients but positively associated with recovery period, increasing from 2.71±0.53 ng/mL at three months to 4.72±0.46 ng/mL at seven months ($p<0.0001$). The study by Holtmann et al. (2020) found that the sex hormones decreased significantly in COVID-19 patients.

Luteinizing Hormone (LH)

Luteinizing Hormone, secreted by anterior pituitary gland, stimulate testosterone production by Leydig cells, several studies have reported that the high levels of LH in COVID-19 individuals, suggesting compensatory responses to reduced testosterone secretion or primary testicular impairment. Ma et al. (2021) noticed higher LH levels and lower testosterone /LH ratio in 119 reproductive -aged male COVID-19 patients compared to 273 age-matched control groups. Another study revealed a higher level of serum LH in patients with active or recent COVID-19 infection compared with healthy controls groups (Cannarella et al., 2024). In recent study, by Majidipour et al. (2025) found significant difference in LH levels between COVID-positive and COVID-negative groups at p value <0.001.

The elevated LH in the context of reduced testosterone suggests primary testicular dysfunction, where the pituitary attempts to compensate for inadequate testosterone production by increasing LH secretion, Leanza et al., 2022). The T:LH ratio has emerged as a useful marker of Leydig cell function, with reduced ratio indicating impaired testicular steroidogenesis (Ashonibare et al., 2024).

Follicle- Stimulating Hormone (FSH)

Follicle-stimulating hormone (FSH), also secreted by anterior pituitary gland, it plays an important role in spermatogenesis process though its action on Sertoli cells. Studies have documented various effects of COVID-19 on FSH levels. A study by Majidipour et al. (2025) showed presence significant difference in FSH levels between COVID-19 positive and COVOD-19 negative groups at ($p<0.001$). Another study by Albayaty et al. (2024), observed that FSH levels were significantly higher post 3 months compared to 5-7 months at ($p<0.0001$), negatively associated with recovery period. While in study conducted by Koc & Keseroğlu (2021) showed no significant changes in FSH levels post COVIID-19 diagnosis.

The variable FSH response may reflect differences in the severity and stage of testicular damage, with elevated FSH indicating Sertoli cell dysfunction and impaired spermatogenesis, while

normal or reduced FSH levels may suggest central (hypothalamic-pituitary) suppression (Cai et al., 2022).

The study by Li et al. (2020), concluded that the imbalance in testosterone, LH, FSH ratio predicts defects in male fertility during SARS-CoV-2 infection, and the impaired Hypothalamic -pituitary gonadal -axis activity can change reproductive hormonal levels and leads to deterioration reproductive function. Furthermore, the physiological stress leads to elevation in oxidative stress (OS) levels in human body and increased OS levels have negative impacts on male reproductive system by inhibition the secretion of male sex hormone.

Other Hormones

Multiple studies have investigated additional male reproductive hormones in study by Cannarella et al. (2024) revealed a higher level of prolactin and 17 β-estradiol hormones in patients with recent or active COIVID-19 infection compared to healthy control groups. while Lan et al. (2024)noted that that the prolactin levels increased by 2.42 ng/ml (p=0.01) and estradiol by 11.88 pg /mL(p=<0.00001) .

Hypothalamic -Pituitary-Gonadal Axis Dysfunction

The pattern of hormonal changes characterized by decreased testosterone, increased LH and variable FSH level suggests primary testicular impairment as the predominant mechanism of HPG axis dysfunction in COVID-19 patients (X. Li et al., 2022). The study by Selvaraj et al. (2021) observed the reduction in testosterone production is correlated with alteration of gonadotropin secretion with studies reporting decreased testosterone levels and altered hypothalamus-mediated gonadotropin secretion (LH and FSH) in COVID-19 positive cases. Harb et al. (2022) noted there are irregular levels of gonadotropin with neuroimaging suggesting hypothalamic abnormalities and an expanded pituitary gland, potentially disrupting gonadotropin release and reduced testosterone levels.

The clinical implications of COVID-19-induced hormonal changes are considerable. Hypogonadisim can contribute to fatigue, decreased sexual desire, erectile dysfunction and deteriorated spermatogenesis process (Yahya et al., 2025).

COVID-19, orchitis and testicular histological changes

Autopsy studies and testicular biopsies from COVID-19 patients have provided critical insights into the direct pathological effects of SARS-CoV-2 on testicular tissue. These investigations have found a spectrum of histological anomalies involved orchitis, inflammatory infiltrates, spermatogenesis disruption, Leydig cell damage, Seminiferous tubules alterations, blood-testis barrier compromise, Vascular alteration, thrombosis and Fibrosis with long -term structural alterations.

Orchitis and Inflammatory Infiltrates

Orchitis, defined as inflammation of the testis has been documented in several autopsy studies of COVID-19 patients. (Duarte-Neto et al., 2022) showed presence mild interstitial orchitis mainly consist of CD68 + macrophage (CD68 is a protein marker expressed on macrophage surface act as inflammatory infiltrate indicated to presence inflammation) and TCD8 + T cells in eight cases of COVID-19 patients. Ma et al. (2021) found many inflammatory infiltrates markers act as immunohistochemical stain to identify the white blood cells causing the inflammation practically orchitis such as CD20+ B lymphocytes, CD3 +T lymphocytes and CD 68 +macrophages in interstitial compartments suggesting viral orchitis and a secondary autoimmune response.

Another study by Peirouvi et al. (2021) revealed high expression of CD68 in interstitial tissue indicating inflammatory infiltrates, with autopsied testicular specimens showing significant alterations in the spatial arrangement of testicular cells and a reduced number of Sertoli cells.

In study by Li et al. (2020) suggested the elevated testicular immune response as cause of testicular damage and impaired sperm parameters, in fact, they detected interstitial congestion, edema and red blood cells at autopsy of epididymal testicular sample from patients who died from COVID-19. additionally, they found elevation in seminal levels of interleukin 6(IL-6) and tumor necrosis factor (TNF-α), origin of autoimmune response of orchitis suggested by these authors.

Another study by Mikhail et al. (2021) observed by scrotal ultrasound presence orchitis and/or epididymitis in approximately 22-42% of men with COVID-19 admitted to the hospital.

Spermatogenesis Disruption

Impaired spermatogenesis represents one of the most consistent findings in autopsy studies of COVID-19 patients. Ma X.et al. 2021 observed abundant degenerated germ cells sloughing into seminiferous tubule lumens, with massive loss of germ cells in some cases, resembling Sertoli cell-only syndrome, indicating impaired male germ cell development and spermatogenesis damage (Ma et al., 2021). The study by Costa et al. (2022) showed disruption of spermatogenesis and blood testis-barrier (BTB) integrity through observation thickening of the tunica propria, germ cell apoptosis and loss of the Sertoli cell barrier. In recent study by Brieno-Enriquez et al. (2026) confirmed a significant decrease in Sertoli cells and spermatogonia stem cells (SSC), with massive DNA damage and apoptosis, with virus disturbance spermatogenesis and modify testicular architecture, also recovered patients showed decrease SSC populations up to 12 months after infection with high DNA damage.

Another study by Li et al. (2020) reported defected spermatogenesis and histological damage in autopsy specimens of epididymis and testis from COVD-19 patients. The mechanisms underlying of impairment spermatogenesis appear to be multifactorial. Direct viral infection of germ cells, inflammatory cytokines, oxidative stress, hypoxia, fever and disruption of the testicular microenvironment all likely contribute (Sengupta et al., 2021).

Leydig Cell Damage

Leydig cells, responsible for testosterone hormone production, have been shown to be vulnerable to SARS-CoV-2 virus and COVID-19-related damage. Duarte-Neto et al. (2022) confirmed decreased Leydig cells and diminished spermatogenesis process. Another study by Costa et al. (2022) found evident Leydig cell inhibition addition to hemorrhage, Inflammation, angiogenesis and fibrosis.

According the study by Rago & Perri (2023) reported reductions of Leydig cells along with interstitial congestion, infiltrated immune cells and micro-thrombosis.

The damage to Leydig cells provides a direct illustration for decreased testosterone levels observed in COVID-19 patients (Li et al., 2023).

Seminiferous Tubule Alteration

Seminiferous tubules are the sites of spermatogenesis process it is show comprehensive changes in COVID-19 patients. Duarte-Neto et al. (2022) reported presence thickening of the tubular basal membrane. Costa et al. (2022) observed thickening of the tunica propria. And in study by Peirouvi et al. (2021) demonstrated dysregulation of junctional proteins such as (occludin, claudin-11, connexin-43) of the blood -testis barrier, disturbance its integrity, all these alterations deteriorating spermatogenesis process and leading to structural changes in seminiferous tubules. As demonstrated by Ly et al. (2023) presence enlargement of testicular tunica propria with plenty of peritubular myeloid cells and collagen fibers in addition to compromised tight junctions between Sertoli cells, detachment of seminiferous epithelium and germ cell degeneration.

Blood -Testis Barrier Integrity

The Blood -testis barrier (BTB), formed by tight junctions between Sertoli cells, is essential for maintaining the immune-privileged environment necessary for spermatogenesis. COVID-19 infection has been shown to compromise BTB integrity by several mechanisms. According to study by Costa et al. (2022) observed loss of the Sertoli cells barrier and indicating impairment BTB integrity.

Ly et al. (2023) confirmed compromised tight junctions between Sertoli cells. Tian & Zhou (2021) speculated that the cytokine storm induced by SARS-CoV-2 plays central role in orchitis and impairment of blood -testis barrier.

The impairment of the BTB has significant impact on fertility by allowing inflammatory mediators and immune cells to inter the seminiferous tubules, leading to autoimmune against sperm antigens (Leanza et al., 2022). This may interpret the existence of anti-sperm antibodies and prolonged spermatogenic impairment observed in some COVD-19 patients (Wang & Xu, 2020).

Vascular Alteration and Thrombosis

Vascular alteration and thrombotic phenomena in testicular tissues have been documented in several studies. Duarte-Neto et al. (2022) observed presence fibrin thrombi in 5 cases with congestion and high expression of vascular cell adhesion molecules (VCAM) protein in vessels. These vascular alterations are likely to cause hypoxia and testicular ischemia, further exacerbating spermatogenic

dysfunction. The study by Rago & Perri (2023) found evident of micro thrombosis. A study published recently by Brieno-Enriquez et al. (2026) observed through it increased immune cell infiltration and thrombosis.

Fibrosis and Long -Term Structural Alterations

Some studies have confirmed fibrotic changes in testicular tissue post -COVD-19 infection, Costa et al. (2022) found evident fibrosis.

A study by Ly et al. (2023) observed presence enlargement of testicular tunica propria with abundant collagen fibers. Fibrosis represents a potentially irreversible alteration that could lead to constant fertility impairment (G. M. J. Costa et al., 2023).

CONCLUSION

This systematic review provides comprehensive evidence that SARS-CoV -2 infection negatively affects male fertility through numerous interconnected mechanisms. The influence of COVID-19 on male reproductive system is multifaceted, including alterations in sperm parameters, hormonal disruption, and direct testicular pathological changes.

1. **Sperm Parameters**: COVID-19 infection significantly impairs multiple sperm parameters according to meta-analysis demonstrating decreasing in sperm volume, sperm concentration(count), total motility particularly progressive motility, and morphology. The extent of impairment appears to associate with infection severity and the presence of fever. Importantly, most studies show partial to complete recovery of sperm parameters within three to six months post infection, corresponding to the duration of the spermatogenic cycle.
2. **Viral Presence in Semen**: SARS-CoV-2 RNA detection in seminal fluid remains relatively rare, and detection rates ranging from 3-8% across studies. Viral presence is most commonly detected during the acute phase of infection, particularly with first 11 days post diagnosis, and is correlated with severe disease and high viral load. The low detection rate, combined with absence of infectious virus particles in most studies, suggests that sexual transmission is unlikely, notably after the acute phase. However, the high expression of ACE2 receptors in testicular tissue indicate that the male reproductive tract is vulnerable to viral effects through mechanisms beyond direct viral replication.
3. **Reproductive Male Hormones**: COVID-19 causes significant hormonal changes characterized by decreased levels of testosterone and increased luteinizing hormone indicating primary testicular disruption, The testosterone/LH ratio serves as a marker to Leydig cell function is consistently decreased in COVID-19 patients. Follicle-stimulating hormones shows variable findings, in some studies reporting elevations in FSH levels and others shows reduction or no changes.in addition to several hormonal changes include elevated prolactin and estradiol levels. Fortunately, most studies show gradual recovery of testosterone levels over 3-12 months after infection, though a subset of patients develops constant hypogonadism requiring long -term monitoring and potential intervention.
4. **Testicular Histopathological changes**: Autopsy studies and testicular biopsy from covid-19 patients concluded comprehensive testicular pathology involved orchitis with inflammatory infiltrates such as (CD68+macrophages, CD3+T cells, CD20+B cells), Leydig cell damage, blood -testis barrier compromise, spermatogenesis deterioration with germ cells loss, seminiferous tubules alterations, vascular alterations with thrombosis in

addition to fibrosis in severe conditions. The disruption of blood- testis barrier integrity through down-regulation of tight junction proteins and up-regulation of inflammatory cytokines provides a mechanism for immune-mediated damage and potential autoimmune responses.

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