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REVIEW

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Semen in the time of COVID-19: a narrative review of current evidence and implications for fertility and reproductive health

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Abstract

Background Historically, viruses have impaired the functionality of human systems. The discovery of novel viruses and the resurgence of established strains heighten concerns about their implications for reproduction. In the aftermath of COVID-19, research efforts have intensified to broaden the understanding of the severe acute respiratory syndrome coronavirus-2's (SARS-CoV-2) effect on male reproduction across diverse populations. Various findings have been reported, with more studies highlighting the adverse impact of SARS-CoV-2 on semen parameters and, consequently, male fertility. This review aims to comprehensively assess and consolidate existing evidence on the impact of SARS-CoV-2 on semen quality and male fertility. It highlights the potential mechanism of action and further underscores the implications for assisted reproductive technology.

Methodology A thorough literature search was conducted across various electronic databases, including PubMed, Scopus, Google Scholar, Embase, and Web of Science. Studies published between January 2020 and May 2024 were included if they explored the impact of SARS-CoV-2 on semen quality.

Results Twenty-nine (29) studies were included in the review. These studies varied in findings but delineated a pattern and trend. While most studies noted a decline in sperm parameters—motility, count, concentration—altered morphology, hormonal imbalances, and increased DNA fragmentation in COVID-19 patients, others reported normal semen parameters 3 to 6 months post-recovery. Few studies reported no change in semen parameters, especially with mild disease. Potential mechanisms underscoring these effects include the presence of fever and consequent release of pro-inflammatory cytokines—interleukin 1β, tumor necrosis factor (TNF), and interferon-gamma (IFNγ). In addition, the activities of the angiotensin-converting enzyme 2 (ACE2) and the transmembrane serine protease 2 (TMPRSS2) receptors have been implicated as gateway mechanisms for viral entry. The long-term consequences and comparisons with other viral infections highlight the complexity of drawing definite conclusions. The different findings on semen changes have implications for assisted reproduction and family planning. Research suggests potential negative effects on gonadal function, emphasizing the need for long-term follow-up studies to understand the persistent effects on male fertility biomarkers.

Conclusion A multidisciplinary approach is essential to optimizing male reproductive health during and after SARS-CoV-2 infection. This includes incorporating assessments into vaccine safety studies to address fertility concerns.

Keywords COVID 19, SARS-CoV-2, Semen, Male fertility, Viral infection

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Background

The COVID-19 pandemic in 2020 launched coronaviruses to the global stage, exposing its historical viral lineage in animal and human populations that was insufficiently explored. The advent of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and the ensuing pandemic highlighted its devastating potential. Reported cases and the documented mortality thereof prompted the World Health Organization (WHO) to declare it a Public Health Emergency of International Concern (PHEIC) on January 30, 2020 [1], and subsequently, a pandemic on March 11, 2020 [2]. Since then, numerous complications have been reported, posing an unprecedented threat to healthcare systems and public health. These comorbid conditions range from mild to severe respiratory, cardiovascular, renal, neurological, and hematological conditions [3, 4]. Although earlier in the pandemic, the respiratory system was thought to be the primary and only target of the virus, long-term effects, and studies have shown that the virus has a propensity to affect other body tissues and organs, including the kidneys, liver, and reproductive organs such as the testes [5, 6]. Recent research has demonstrated that the testes are another organ significantly affected by the virus, thereby raising concerns about its potential effects on male reproductive health.

In the pre-SARS-CoV-2 era, about 27 viruses have been found in human semen, negatively impacting sperm quality and male fertility. However, in most cases, there is limited evidence regarding their potential for sexual transmission [7]. The impact of the COVID-19 virus on male infertility has been investigated and documented. Studies have highlighted male infertility as one of many complications of coronavirus infections [8–11]. The virus compromises the male reproductive system through direct viral replication within the testes, resulting in cellular damage and indirect immunopathological effects that disrupt spermatogenesis and hormonal balance [12]. The evidence of an associated hormonal variance among infected males was strengthened by the results of Wang S et al., which reported a drastic reduction in the testosterone-to-luteinizing hormone ratio among COVID-19 patients—a pointer to the possible response of the Leydig cells to the effect of the luteinizing hormones [13].

The aetiopathogenesis of SARS-CoV-2 is similar to other viruses. Abnormal sperm morphologies and DNA damage, with inflammation and testicular atrophy seen in HIV-1, human papillomaviruses (HPV), Zika, and the Mump viruses, have also been reported in SARS-CoV-2 studies [14]. With research uncovering the extrapulmonary impact of SARS-CoV-2 infections and rising rates of male infertility, studies have explored the adverse potential of the virus on the male reproductive system, and insightful findings have been reported. This narrative review aims to provide a comprehensive understanding of the effects of SARS-CoV-2 infection on male fertility. It synthesizes current evidence assessing the impact of the virus on semen parameters while investigating the potential mechanisms by which the virus invades and impairs reproduction in this population.

Methodology

Search strategy

The literature used in this review was sourced across multiple electronic databases—PubMed, Google Scholar, Embase, and the Web of Science. The search on PubMed utilized Medical Subject Headings (MeSH) terms. The search used keywords such as "COVID-19," "SARS-CoV-2," "male infertility," "semen," "semen analyses," "semen quality," "semen parameters," and "virus" combined in search strings using Boolean operators (AND/OR). An additional search through the reference lists of the included papers provided more studies for review. The search was conducted in May 2024 and restricted to articles published from January 2020 to May 2024 to maintain currency in synthesized information.

Eligibility criteria

Studies were considered for the review if they were published in full-text format and written in the English language. They should have investigated the effects of the SARS-CoV-2 on male infertility using semen analysis, included at least one quantitative outcome measure of semen quality or parameters, and were conducted between January 2020 and May 2024. Studies not meeting the above criteria or reporting the effect of other viruses on male infertility were excluded from the study. Additionally, editorials, reviews, commentaries, and opinion articles were excluded.

Data extraction and synthesis

Selected studies were further assessed for eligibility by two authors who independently reviewed the titles and abstracts of all retrieved papers. The authors conducted an independent selection of the documents, discussed the findings with each other, and crosschecked disparities with other authors. The selected studies were subjected to data extraction with essential data, such as author name, publication year, study aims and location, study design, and size, COVID-19 testing method, method of semen collection and analysis, main findings, study limitations, and recommendations, were summarized into data extraction table (Table 1). Content analysis was done on the extracted data, and identified themes were discussed accordingly. Qualitative synthesis was conducted

Table 1 Studies discussing the impact of COVID-19 on semen quality and male fertility

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Guo et al. (2021) [8]	Case–control study 41 men	To ascertain the consequences of COVID-19 on sperm parameters after recovery (Anhui Province, China)	Throat swabs or respiratory specimens by RT-PCR assay	Semen samples were obtained by masturbation. Sperm concentration and sperm motility were assessed by computer-assisted sperm analysis (CASA) under phase contrast microscopy	Reductions in total sperm count, sperm concentration, and mobility in patients who had recovered from COVID-19 after hospitalization	Using CASA, an optional choice for semen analysis	Long-term follow-up studies be conducted on more patients and elucidation of the underlying pathological mechanism explaining the after-effects of COVID-19 on spermatogenesis
Aksak T et al. (2022) [9]	Case–control study 200 men aged 20–50 years	To compare the sperm parameters of individuals with and without COVID-19 and to investigate the effect of COVID-19 on sperm parameters (Ministry of Health Adana City Training and Research Hospital in vitro fertilization (IVF) unit andrology laboratory)	Positive PCR test	Sperm analysis was analyzed per WHO (WHO, 2010) criteria	Sperm concentrations of COVID-19 patients decreased significantly compared to the control group. Additionally, sperm counts of the patients with moderate signs of infection were lower than those who survived a mild infection. No statistically significant difference was recorded for volume change, motility, and morphological difference	Small sample size	Long-term studies with larger samples (comparative before and after COVID-19) to better understand the changes in sperm concentration values are required
Hu B et al. (2022) [10]	Case–control 36 cases and 45 controls	To assess the mid- and long-term impact of COVID-19 on the quality of male semen (China)	Real-time RT-PCR assay of pharyngeal swab specimens	Semen samples were obtained by masturbation and ejaculation directly into noncytotoxic sterile containers. Analysis was done according to the WHO laboratory manual for the examination and processing of human semen	Semen quality of COVID-19 recovered patients was impaired during the early period; however, it improved after a recovery time of nearly half a year. In addition, the total sperm number had an improvement after a recovery time of about 150 days	-Sample size was relatively small, especially for exploring the alterations of semen parameters with time -Sperm analysis of participants performed before the infection of COVID-19 was not obtained, which cannot entirely exclude the possibility of pre-existing infertility	A larger cohort study with different recovery time is required for confirmation and exploring the specific time at which sperm quality began to improve

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Scroppo et al. (2021) [11]	Prospective study 15 men aged 18 to 50 years	To evaluate the possible presence of SARS-CoV-2 in semen samples and to define the semen quality in sperm collected from young Italian men with COVID-19	SARS-CoV-2 positive oropharyngeal swab	The sample was produced on-site by masturbation into a sterile plastic specimen cup following abstinence of 2–7 days according to WHO 2010 Liquefied semen samples were analyzed under the light microscope at 200× magnification using Makler's counting chamber	Changes in the seminal fluid were seen in almost all patients, but no associations were found with inflammation indices. The presence of SARS-CoV-19 viral RNA within the seminal fluid was excluded. Most of the patients studied had exhibited alteration of the seminal fluid	Relatively low number of sample patients studied	Further investigation and monitoring of COVID-19 patients for potential reproductive health implications, given the observed alterations in seminal fluid characteristics and the absence of viral RNA in semen samples
Donders GGG et al. (2022) [21]	Prospective cohort study 120 men	To determine if SARS-CoV-2 could be detected in semen of adult men who had recovered from COVID-19 infection (Belgium)	Nasopharyngeal SARS-CoV-2 RT-PCR	Sperm sample obtained by masturbation into noncytotoxic sterile containers. All sperm samples were analyzed following the WHO guidelines for semen analysis	Substantial reduction in sperm concentration, the number of spermatozoa produced, and both total and progressive motility of the spermatozoa after COVID-19 infection. SARS-CoV-2 RNA was not detected in semen during the period shortly after infection nor later	Had no comparative sperm samples from the participants before they contracted COVID-19, nor did the study to include samples from matched control men without COVID-19	Introducing a follow-up period of 6 months as an amendment to the study will provide specific detailed information on the mechanisms of recovery of sperm quality over time
Piroozmanesh H et al. (2021) [23]	Case–control study 100 males	To investigate the impact of COVID-19 infection on sperm parameters and reproductive hormones in fertile men (Infertility Treatment Centre of Qom, Iran)	Nasopharyngeal swab test for COVID-19 and positive IgM and IgG antibodies	Masturbation and ejaculation directly into noncytotoxic sterile containers Eosin-nigrosine staining was used to analyze the viability of sperm	Reduced concentrations and sperm viability, alterations in morphology, diminished motility, enhanced DNA fragmentation, and significantly decreased TAC among those with good reproductive function and concomitant COVID-19 infection	Small sample size	To conduct clinical evaluations, including assessments of hormonal and semen parameters, particularly in severe cases. Proactive monitoring and intervention strategies can help safeguard male reproductive health during infection

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Erbay G et al. (2021) [24]	Retrospective cohort study 69 patients aged 20–45 years	To investigate the effect of COVID-19 on spermatogenesis	RT-PCR test of combined oropharyngeal and nasopharyngeal swabs	Semen samples obtained by masturbation were examined manually under a microscope according to the WHO 2010 criteria within 30 min after being liquefied at room temperature	Progressive and total motility and vitality decreased compared with the pre-disease period in the mild symptomatic groups. Conversely, in the moderate symptomatic, all the sperm parameters were negatively affected by the disease	-Sperm morphology and leukocyte count could not be analyzed in some of the centers, and were excluded from the assessment in order to ensure standardization - Only one spermiogram test was performed and compared for each patient before and after COVID-19	Long-term and multicenter studies with larger sample sizes
Depuydt C et al. (2023) [25]	Observational prospective cohort study 120 patients aged 18–70 years	To analyze the differential effect and the impact of SARS-CoV-2 infection on different semen quality parameters (Antwerp, Tienen or Genk, Belgium)		Fresh sperm sample produced by masturbation. Sperm quality was assessed using WHO guidelines	Deleterious effects of the viral infection on the production of male gametes	Not having a control group before infection of the case group	N/A
Ma L et al. (2020) [26]	Case–control 392 Men	To compare the sex-related hormones between 119 reproductive-aged male COVID-19 patients and 273 age-matched uninfected men (Wuhan Leishenshan Hospital)	qRT-PCR of nasal and pharyngeal swab specimens or by serum virus antibody (IgM or IgG) detection using the colloidal gold test	Semen samples were obtained by masturbation after an abstinence period of 2 ~ 7 days (with a median of 4 days) and processed within 1 h of ejaculation for analysis. Semen assessment was performed according to WHO criteria	Abnormal sex hormone secretion among COVID-19 patients. No SARS-CoV-2 virus was found in semen from recovering COVID-19 patients	-All samples were collected from mildly affected patients and were in the recovery stage - The sample size for semen assessment was limited	- Longitudinal studies to determine if COVID-19-related gonadal dysregulation is transient or prolonged - Explore underlying mechanisms of gonadal dysfunction in COVID-19 patients - Include semen examination in gonadal function evaluation for men who recovered from COVID-19

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Paoli D. et al. (2022) [27]	Case–control study 80 men	To investigate whether SARS-CoV-2 infection affects male reproductive health (Italy)	Nasopharyngeal swab positive for SARS-CoV-2	Semen samples were collected by masturbation after 2–7 days of abstinence. All samples were allowed to liquefy at 37 °C for 60 min and were then assessed according to WHO 2010 criteria	The virus does not seem to cause direct damage to the testicular function, while indirect damage due to inflammation, drugs, and fever appears to be transient	The absence of pre-infection data	- Conducting longitudinal studies to assess the long-term impact of COVID-19 on sexual health - Incorporating multi-disciplinary approaches to explore the interplay between COVID-19 and sexual functioning - Implementing standardized assessment tools to accurately evaluate post-COVID-19 sexual dysfunction
Morselli S. et al. (2021) [28]	Prospective cohort study 43 men	To evaluate a panel of inflammatory mediators in semen in patients recovered from coronavirus disease 2019 (Italy)	Swabs for SARS-CoV-2 RNA	Semen samples were collected by masturbation after 2–7 days of abstinence. All samples were allowed to liquefy at 37 °C for 60 min and were then assessed according to WHO 2010 criteria	Patients with COVID-19 might have high levels of pro-inflammatory cytokines in seminal plasma, particularly for patients with severe impairment of semen parameters	-Small study sample -Low number of patients with available serum procalcitonin data	Further studies to evaluate whether inflammatory process persists after a longer period from recovery as well as to clarify SARS-CoV-2's mechanisms of action on the male genital tract
Cakir C. et al. (2023) [29]	Retrospective cohort study 342 men	To investigate the effect of SARS-CoV-2 on semen parameters by comparing semen analyses before and after COVID-19 diagnosis in the same patient	Positive RT-PCR test	Semen samples were obtained through masturbation; further analysis were conducted according to WHO guidelines	Semen volume, sperm count, motility, and morphology decreased post-infection. Fever during infection negatively impacted sperm concentration	Absence of pre-COVID-19 spermiogram results and insufficient comparison of post-infection semen parameters with a control group	More studies should be conducted with a larger Sample Size

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Holtmann N et al. (2020) [30]	Prospective cohort study 34 men	To investigate the presence of viral RNA in human semen of patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and to evaluate its presence and relevance in semen parameters (University Hospital in Duesseldorf, Germany)	Positive swab result (ESwab collection kit; Copan) or positive Immunoglobulin (Ig) A and IgG antibodies	Semen sample of each participant was obtained by means of masturbation and ejaculation directly into noncytotoxic sterile containers. Freshly collected semen was liquefied for 30–60 min at room temperature and processed within 1 h of ejaculation for analysis of sperm per by WHO criteria	SARS-CoV-2 RNA was not detected in semen samples from neither recovered nor acute infected subjects. There was reduced semen volume, concentration, decreased total number of sperm per ejaculate, decreased progressive motility, decreased immotile cells, and decreased leucocytes. Parameters were worse with patients with moderate disease compared to those with mild disease and the controls	Relatively small sample size. Sperm analysis of study participants before the pandemic was not obtained, limiting the diagnosis of pre-existing male infertility. Also, only two patients with an active disease were analyzed. Preliminary results lack any data about long-term effects of SARS-CoV-2 on male reproductive function	To ascertain and corroborate findings in a larger sample size, especially among those with active disease
Ali AM et al. (2023) [31]	Comparative study 51 men	To assess the effects of SARS-CoV-2 on semen parameters by comparing samples during and after infection in the same patients	SARS-CoV-2 from throat swab by RT-PCR	Semen samples were collected by masturbation into a sterile container after 3–5 days of sexual abstinence Semen analysis performed according to the WHO 2010 guidelines	Significant adverse impacts on various parameters during COVID-19 infection. Additionally, total count, total motility, and sperm morphology were negatively affected. Hormone levels were lower during infection, likely due to increased inflammatory cytokines, but returned to normal post-recovery	1. Small sample size 2. Absence of pre-infection semen analysis profiles	To conduct larger-scale studies to gain deeper insight into the long-term consequences of COVID-19 on sperm parameters and fertility, ensuring more accurate assessments

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Törzsök P. et al. (2023) [32]	Cross-sectional study 31 men	To evaluate the effect of COVID-19 infection on male fertility including oxidative stress, and sexual function (University Clinic of Urology and Andrology Salzburg)	Nasal COVID-19 PCR test	Semen samples were collected in the hospital by masturbation after 2–5 days of sexual restraint. All samples were analyzed within one hour after collection, in accordance with the WHO criteria 2010	All post-COVID-19 testosterone levels were within the normal range; however, pre-COVID-19 testosterone values, available for six cases showed COVID-19 infection had no negative impact on spermiogram parameters	Limited pre-pandemic lab data, small sample size, and varying follow-up periods prevented accurate assessment of immediate short-term COVID-19 impact on sperm parameters. Inconsistent vaccination regimens also hindered reliable evaluation	The study suggests that COVID-19 infection does not significantly impact sperm quality or oxidative stress within 90 days after symptom onset. However, the presence of anti-sperm antibodies (ASA) and new-onset erectile dysfunction post-COVID-19 should raise concerns and warrant further investigation
Enikeev D. et al. (2022) [35]	Prospective study 88 men 18–65 years	To investigate the effect of SARS-CoV-2 on testicular function, hormone levels and determining the extent of impact on spermatogenesis and damage to testicular tissue (COVID-19 Hospital of Sechenov University, Moscow, Russia)	Chest CT scan, confirmed with nucleic acid detection of SARS-CoV-2 throat swab using RT-PCR	N/A	The semen analysis revealed decreased motility in COVID-19 patients, and a higher number of immobile sperm. All parameters returned to normal at 3 months after discharge	Small number of participants and the absence of data on those in whom both the sperm test and pathology results are available	Future studies should aim to recruit a larger sample size to improve the generalizability of findings and enhance statistical power - It is essential to gather data on both sperm test results and pathology findings for all participants to provide a more comprehensive understanding of the impact of COVID-19 on fertility

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Edimiris P. et al. (2023) [36]	Prospective case–control study 37 men	To clarify whether mild COVID-19 has an impact on sperm parameter values, how long this impact lasts, and whether vaccination can prevent deterioration of sperm quality (Duesseldorf, Germany)	SARS-CoV-2 from throat swab by RT-PCR	The ejaculate was collected by masturbation into a sterile cup RNA was extracted from semen samples using the EZ1 Virus Mini Kit according to the manufacturers' protocols	Semen parameter values did not differ significantly between mild COVID-19 patients and the control group. Serial examination revealed no significant changes in semen parameters at 4, 18, and 82 days after symptom onset. No SARS-CoV-2 RNA or infectious particles were detected in any ejaculate	Insufficient hormonal analysis and andrological examinations, as well as a small sample size due to participants' reluctance to provide ejaculate in the acute stage of the disease	N/A
Stigliani S. et al. (2023) [37]	Longitudinal retrospective study 20 men	To investigate whether COVID-19 disease has a negative impact on semen parameters and male reproductive potential after recovery (San Martino, Genova, Italy)	Nasopharyngeal swab for SARS-CoV-2 infection	Semen samples were collected by masturbation in a sterile container after 2–5 days of abstinence. The basic analysis, including semen volume, sperm concentration, and motility, was performed following WHO guidelines	Semen parameters did not reflect any detrimental effect of COVID-19 disease. In addition, no influence of COVID-19 infection on the performance of male patients in their subsequent infertility treatments	Small sample size - Lack of long-term follow-up as well as data on live childbirth and further cumulative pregnancy outcomes - Most participants had mild clinical symptoms, which may not account for the exact impact of SARS-CoV-2 on fertility treatment results	More extensive studies with a longer follow-up will be needed to confirm this study results and to determine whether permanent harmful effects may occur in a minority of men

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Martinez MS. et al. (2023)[38]	Prospective cohort study 231 men	To compare inflammatory markers, leukocytes in semen, and sperm quality in 231 men who recovered from mild or severe COVID-19 to 62 healthy unvaccinated men	Nasopharyngeal swab for SARS-CoV-2 infection	Semen samples were collected by masturbation into a sterile container after 3–5 days of sexual abstinence Semen analysis was performed according to the WHO 2010 semen analysis manual	Elevated levels of IL-1β, TNF, and IFNγ were found in the semen of individuals who had recently recovered from mild and/or severe COVID-19, suggesting inflammation in the semen. Additionally, these individuals showed reduced semen volume, lower total sperm counts, and impaired sperm motility and viability	N/A	N/A
Temiz MZ et al. (2020) [41]	Prospective, cross-sectional, analytical study 55 patients and 10 controls	To investigate whether COVID-19 has any deleterious effect on the male reproductive system and to assess the impact of COVID-19 treatment protocol (hydroxychloroquine, azithromycin, and low-molecular-weight heparin (LMWH)) on semen parameters and the male sex hormone profile (Turkey)	Identification of SARS-CoV-2 RNA extracted nasopharyngeal and oropharyngeal swabs with real-time RT-PCR assay in a genomic laboratory	Semen samples were obtained by masturbation. Ejaculate was collected into a sterile wide-mouthed calibrated container after sexual abstinence period of two to five days. Semen analysis was performed according to WHO Laboratory Manual for human semen exam (5th ed.)	COVID-19 may cause decrease in semen morphology due to the fever instead of the direct effect of SARS-CoV-2 on testes. Significantly decreased serum testosterone, FSH and LH levels with similar PRL levels in COVID-19 patients was found when compared to normal controls	- Relatively small sample size - No investigation of testicular histology - Lack of the long-term results	The findings of this study underscore the importance of further investigation with confirmed tissue analysis and sustained long-term monitoring to provide a comprehensive final assessment

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Wang M. et al. (2022) [45]	Retrospective cohort study 148 patients (unexposed) 50 patients (exposed)	To evaluate the influences of SARS-CoV-2 infection on semen parameters and investigate the impact of the infection on in vitro fertilization (IVF) outcomes (Tongji Hospital, Wuhan)	Serum SARS-CoV-2 antibody tests and PCR tests for detecting SARS-CoV-2 RNA	Freshly ejaculated semen samples were obtained by masturbation and ejaculation into sterile containers after 2–7 days of sexual abstinence. Samples were analyzed according to the published WHO criteria—A combination of manual Papanicolaou sperm staining and CASA system was applied for semen analysis	Morphology percentage of the sperm and number decreased since the pre-disease period, but all parameters remained normal. IVF data showed that male SARS-CoV-2 infection might not affect clinical outcomes, but it led to a decrease in blastocyst formation and availability, suggesting a potential negative impact on embryonic development competency	-A single-center retrospective cohort study with a limited sample size -Patients had only undergone one semen analysis before and after the infection - Only semen analysis was used for evaluating male fertility -The lack of data on live birth and cumulative pregnancy outcomes	A multicenter long-term investigation with a larger sample size More data on other evaluation indices are needed for comparison
Yang T. et al. (2021) [59]	Retrospective observational study 1991 semen samples	To evaluate the impact of air pollution exposure on semen quality parameters during COVID-19 outbreak in China, and to identify potential windows of susceptibility for semen quality (China)	N/A	Semen collection and analysis followed the WHO 2010 procedure	Exposures at different stages of spermatogenesis had varying effects. Late-stage exposure to particulate matter, O3, and NO2 showed a weak but positive association with semen quality. In contrast, late-stage exposure to CO had an inverse relationship with sperm motility parameters. Additionally, exposure to SO_2 seemed to influence semen quality throughout spermatogenesis	-Study lacked information on indoor environmental quality, which could play a major role in individual's exposure profile during the lock-down period -Study did not correct outcomes for confounding factors such as sleeping schedule and diet	N/A

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Pazir Y. et al. (2021) [60]	Prospective cohort study 24 male patients	To investigate the possible effects of SARS-CoV-2 infection on semen parameters in men recovering from COVID-19 In a tertiary academic center	RT-PCR test of pharyngeal and nasal swabs	Semen samples were obtained from the participants by masturbation after a 3-day abstinence period during the recovery phase of COVID-19. All semen analyses were carried out by the same andrology laboratory according to the WHO 2010 guidelines	Sperm motility and total motile sperm count were the same. Semen parameters showed a significant reduction in cases with a history of mild COVID-19	The study included a small, homogenous sample of participants who had recovered from mild COVID-19. Only one semen analysis was conducted after recovery. We did not assess the impact of COVID-19 on other sperm quality parameters, such as oxidative stress and DNA fragmentation	Since most patients recovering from COVID-19 are of reproductive age, periodic monitoring of these patients for reproductive health might be beneficial
Hajizadeh MB et al (2021) [61]	Prospective longitudinal cohort study 189 participants—24 male patients, 105 control	To address the connection between changes in multiple seminal biomarkers and reproductive function in male patients recovering from COVID-19 Masih Daneshvari Hospital, Tehran, Tehran province, Iran	Positive result for SARS-CoV-2 in the qRT-PCR assay of nasal and pharyngeal swab specimens	Semen samples were collected into a sterile container by masturbation. Semen analysis was performed in accordance with the WHO 2010 guidelines for the examination of human semen	Infection induces impairments in the male reproductive function, marked with an overproduction of the seminal markers of inflammation and oxidative stress as well as the activation of apoptotic variables	Could not carry out the analysis based on the severity of disease for the mild type, as the number of patients in this category was inadequate	Further studies among bigger cohorts with prolonged follow-up periods to investigate the consequences of COVID-19 infection on the male reproductive function
Shi S. et al. (2023) [62]	Prospective cohort study 132 men	To analyze and compare the DNA fragmentation index (DFI) and other sperm parameters between COVID-19 positive and negative groups First Affiliated Hospital of Nanchang University	Nasopharyngeal swab for SARS-CoV-2 infection with existing test record	Semen samples were obtained through masturbation and conducted further analysis according to WHO guidelines	Semen quality was significantly affected during COVID-19 infection. Semen concentration, progressive motility, motility, especially sperm DFI decreased significantly, which had a greater impact on male fertility	Absence of pre-COVID-19 spermiogram results and comparison of post-infection semen parameters with a control group; lack of normal distribution in pre-COVID-19 semen parameters of patients	Longitudinal study focusing on the long-term impacts of COVID-19 in men to uncover underlying mechanisms and devise effective mitigation strategies

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Shcherbitskaia AD et al. (2023) [63]	Prospective cohort 137 men	To investigate the impact of COVID-19 on men's reproductive health, focusing on sperm parameters and testicular inflammation, and examining age-related differences		Masturbation into a sterile non cytotoxic container after 3–5 days of sexual abstinence based on WHO guidelines 2010	Younger patients' post-infection showed higher round cell count in semen and reduced sperm hyaluronan binding ability, while seminal plasma zinc levels and nitrotyrosine in cell fraction decreased in these patients. Sperm DNA fragmentation, total antioxidant capacity, and inflammatory cytokines (IL-1β and IL-10) increased in men over 35 years of age after COVID-19 infection. IL-1β concentration decreased over time in all patients following recovery	Relatively small sample size. The inability to retrospectively evaluate COVID-19 patients and a lack of baseline semen quality data prior to disease onset were other limitations	Future investigations with larger patient cohorts in a variety of age groups are necessary to validate the Findings of this study
Kumar T. et al. (2023) [64]	Cross-sectional observational study 239 men	To compare the semen parameters of men who presented for semen analysis during the COVID-19 pandemic with those of men who presented for semen analysis before the pandemic Andrology Laboratory of All India Institute of Medical Sciences (Patna, India)	Nasopharyngeal swab for SARS-CoV-2 infection	Semen samples were obtained by masturbation in the laboratory facility; the samples were collected in sterile and nontoxic containers. Semen analysis was conducted manually, in accordance with WHO recommendations	Apart from sperm morphology, semen quality parameters showed improvement in the pandemic group compared to the pre-pandemic group	N/A	Further exploration is necessary to understand the factors influencing these variations

Table 1 (continued)

Author and year	Study design and sample size	Study aim (location)	COVID-19 testing method	Method of semen collection and analysis	Main findings	Study limitations	Recommendations
Matzkin ME et al. (2023) [65]	Retrospective cohort study N/A	To analyze semen parameters, oxidative profile, and the seminal fluid prostaglandin and polyamine systems in samples collected from individuals without COVID-19 diagnosis and men who recovered from COVID-19	SARS-CoV-2 from throat swab by RT-PCR	Semen samples were obtained by masturbation with a period of sexual abstinence of 2–5 days transported at body temperature. Other analysis as per WHO guidelines	In both groups of semen samples, sperm vitality, total and progressive sperm motility, and putrescine levels were significantly decreased when compared with control. In contrast, lipid peroxidation, leukocyte-associated cyclooxygenase 2 expression, and prostaglandin D2 levels were higher in semen from coronavirus disease 2019 recovered men than in samples from uninfected individuals	N/A	N/A
Ali BR. et al. (2023) [66]	Prospective cohort study 318 men	To evaluate the SARS-CoV-2 infection severity effects and vaccination on the fertility of males	Positive RT-PCR test	Semen samples were collected by masturbation into a sterile container after 3–5 days of sexual abstinence in accordance with WHO guidelines 2010	The severity of COVID-19 impacts fertility and sperm parameters, particularly progression and sperm morphology, even though these parameters are unrelated to vaccination	N/A	N/A

TAC total antioxidant capacity, *CASA* computer-assisted sperm analysis, *RT-PCR* reverse transcription polymerase chain reaction, *N/A* not available on analyzed studies, and information was integrated to present a comprehensive review.

Results

Overview

A comprehensive summary of the key findings from the 29 included studies included in this review is presented in Table 1 [8–11, 21, 23–32, 35–38, 41, 45, 59–66]. Most studies reviewed were prospective cohort studies conducted between 2021 and 2023. Additionally, case–control, retrospective cohort, and cross-sectional studies were included. This review included studies with a broad range of sample sizes, with the number of participants varying from as few as 20 to approximately 342 men. The age of the study participants ranged from 20 to 65 years old. SARS-CoV-2 status of study participants was confirmed via a reverse transcriptase polymerase chain reaction (RT-PCR) assay conducted on nasopharyngeal/oropharyngeal swab specimens. Few studies reported an additional confirmatory chest X-ray study. Semen samples were collected and analyzed per the World Health Organization guidelines 2010 [42].

Potential mechanism

SARS-CoV-2 interacts with receptors in testicular tissue, potentially triggering an immune response that adversely affects spermatogenesis [6]. The virus induces overexpression of pro-inflammatory cytokines—TNF-α, IFN-γ, and interleukins 1β, 6, 8, and 10—in seminal plasma [38]. This disrupts the regulation of blood-testis-barrier proteins such as claudin-11, occludin, and connexin-43. Additionally, apoptotic genes like caspase-3, caspase-8, caspase-9, and BAX are overproduced in the semen of infected men, along with mature T lymphocytes, B cell-derived immune cells, and macrophage-induced immune cells. This overexpression of cytokines and inflammatory mediators, induced by SARS-CoV-2, alters the normal spermatogenetic microenvironment causing significant inflammation and oxidative stress [17, 18]. The entry of the SARS-CoV-2 virus into the cell is regulated by the angiotensin-converting enzyme 2 (ACE2) receptors which act as the primary entry portal for the virus [19]. These receptors are widespread in the human body; however, they are particularly abundant in the intestinal epithelial cells of the gut, alveolar cells of the lungs, spermatogonial stem cells, seminiferous duct cells of the testis, as well as the endothelial and smooth muscle cells of the blood vessels. Additionally, they are also found in significant amounts in the heart's epicardium, adipocytes, fibroblasts, myocytes, the brain, and the tubular epithelial cells of the kidneys [20]. In the male reproductive system, they are widespread in the spermatogonia, testes, seminiferous duct cells, Sertoli, and Leydig cells, and serve as the gateway for the SARS-CoV-2 [16, 20, 21].

The entry of the virus into the host cells is mediated, as SARS-CoV-2 must first attach itself to the ACE2 surface receptor, where it proceeds to invade the intracellular endosomes, and subsequently fuses its membrane with lysosomal membranes [20]. The virus is characterized by a trimeric spike protein that consists of two homologous domains—S1 and S2. These proteins primarily occupy the receptor-binding domain (RBD), which changes position regularly pending the cellular activity, whether receptor binding or immune invasion. These spike proteins are essential for virus-receptor interaction and subsequent viral entry into the cell [22]. However, prior to binding with ACE2 receptors, the proteins are primed and cleaved by proteases, such as cathepsin L/B and TMPRSS2, at the S1/S2 boundary. Cleavage is facilitated by the protease furin [19, 20, 22], which culminates in the exposition of the S1 C-terminal domain (CTD), enabling the virus to make contact with the peptidase domain of the organ's ACE2 receptors [22]. This virus infects the testes and attaches to the ACE2 receptors expressed on testicular cell types, including seminiferous duct cells, spermatogonia, Leydig cells, and Sertoli cells, subsequently altering the machinery of sperm production. The binding alters the gene expression patterns within these cells and disrupts the normal physiology of sperm development and hormone production. Another receptor, the transmembrane serine protease 2 (TMPRSS2) expressed on the acrosomal region of spermatozoa, has been shown to have a great affinity for SARS-CoV-2 and has been reported as another potent entry point for the virus into the testes [6, 16].

Effect of SARS-CoV-2 on semen quality

Similarities have been observed between SARS-CoV-2 and other viruses known to disrupt spermatogenesis. These viruses can impair various spermatogenic mechanisms, potentially leading to male infertility. Studies report that the SARS-CoV-2 disrupts the regulation of the angiotensin-converting enzyme-2 (ACE2) gene in the testes, resulting in immediate changes in testicular tissues and, consequently, sperm quality and function [21]. The ACE2 enzyme is expressed in the four testes-specific cell types—seminiferous duct cells, spermatogonia, Leydig, and Sertoli cells [21]. Piroozmanesh et al. reported adverse effects on sperm quality, including reduced concentrations, altered morphology, and enhanced DNA fragmentation in COVID-19-infected cases [23]. Concurrently, the study by Aksak T et al. found a significant decrease in sperm concentrations among COVID-19 patients, especially those with moderate symptoms [9]. Long-term and self-limiting evidence of a significant reduction in sperm count, motility, and sperm concentration has been reported [7, 10, 24, 25]. Although a link between COVID-19 infection and a reduction in semen quality and sperm function has been established, expression of the virus in the semen samples of infected patients has yielded conflicting results [11, 21, 32]. The study by Ma L. et al. reported abnormal sex hormone secretion among patients who had recovered from SARS-CoV-2 infection; however, no viral strains were found in semen on analysis [26]. The mechanisms for this are diverse, with various hypotheses reported. An Italian multicentre study reported that the SARS-CoV-2 infection causes transient damage to the male reproductive system from chronic inflammation and resultant persistent fever during and after COVID-19 recovery [27].

Changes in sperm parameters following COVID-19

According to Piroozmanesh et al., individuals with COVID-19 infection who previously had normal reproductive functions were reported with poor semen quality, evidenced by reduced sperm concentrations, viability, altered morphology, decreased motility, increased DNA fragmentation, significantly lower total antioxidant capacity (TAC) and a substantial reduction in reproduction hormones when compared to their non-infected counterparts [23]. A similar study reported changes in semen quality among individuals infected with SARS-CoV-2. It found that 4 out of 100 men in the COVID-19-positive group, who previously had normal hormone levels, developed azoospermia. However, prior sperm analysis results across both study groups were not available for a comparative analysis [9]. Additionally, the sperm concentrations of those with COVID-19 were significantly lower than those in the control group, with variations based on infection severity. However, no statistically significant difference was noted between the two groups in terms of volume, motility, and morphology [9]. Concurrently, a Chinese study by Guo TH revealed temporary reductions in total sperm count, concentration, and motility after SARS-CoV-2 infection [8]. Hu et al. suggested an initial impairment of sperm quality in COVID-19-recovered patients, which resolved after a recovery period [10]. Fabrizio Scroppo et al., in their 2021 prospective study, reported reduced sperm motility and concentration with abnormal morphology in 87% of the study population. Semen viscosity was increased in 80% of the patients with normal leucocyte parameters. Notably, SARS-CoV-2 RNA was not reported in any of the investigated semen samples [11]. Depuydt et al., in their latest 2023 follow-up study of 93 patients who had recovered from COVID-19, reported that SARS-CoV-2 infection has a negative impact on various sperm parameters. In addition to the direct fatal effects of the virus on the production of male gametes, it also showed that the virus deactivates finished spermatozoa by impairing their motility and sperm DNA [25]. Patients infected with SARS-CoV-2, particularly those with severely compromised semen quality, may exhibit fever and elevated levels of pro-inflammatory cytokines such as IL-1β, TNF, and IFNγ in their seminal plasma [28–31, 38]. In addition, Ma X. et al. reported thinning of seminiferous tubules, oligozoospermia, degenerated germ cells, and altered transcriptome [33]. To support existing findings, postmortem examinations conducted within 1 h of death on 12 COVID-19-diagnosed patients at Tongji Medical College Hospital, China, revealed severe fibrosis in testicular specimens [15]. Morphological changes were noted in seminiferous tubules of other samples and included vacuolation, swelling, and cytoplasmic rarefaction of Sertoli cells. Significant intratubular cell mass sloughing into lumens, interstitial edema with inflammatory infiltrates of CD3-positive T lymphocytes, fewer sperm cells, and significant germ cell death have been reported in this and similar studies [15, 34].

Contrasting findings

Few studies have noted opposing findings. Törzsök P et al. reported normal level post-COVID-19 testosterone levels; however, pre-COVID-19 data available for a small number of study samples suggested that COVID-19 infection did not negatively impact sperm quality as measured by standard semen parameters [32]. In addition, Edimiris et al. found that semen parameter values did not differ significantly between mild COVID-19 patients and the control group. Serial investigation of semen samples revealed no significant changes in semen parameters at 4, 18, and 82 days post-onset of COVID-19 symptoms [36]. The study also reported no SARS-CoV-2 RNA or infectious viral particles detected in any of the assessed ejaculates [36]. In their study, Stigliani et al. noted similar findings, observing that SARS-CoV-2 infection did not affect semen parameters or long-term fertility status [37]. According to Paoli et al., the virus exerts no direct adverse effects on testicular function, although indirect effects due to fever, drugs, and inflammatory outcomes are usually self-limiting [27].

Discussion

The results of this review show the adverse effect of SARS-CoV-2 on semen parameters and further expound on its potential impact on male fertility. Semen changes in individuals affected by COVID-19 and their relationship with fertility are complex. While most findings have supported a negative impact with reduced semen quality, other studies have reported these changes to be temporary, with sperm quality returning to normal levels within a few months of recovery [14, 35], or no significant impact on semen parameters or fertility [36, 37]. These opposing views still pose a grey understanding of the cognate potential of the virus on male fertility. The mechanisms underlying these changes are still being investigated, but they might be related to systemic inflammation and resultant cytokine activity or hormonal imbalances caused by the virus. Martinez et al. reported elevated levels of IL-1β, TNF, and IFNγ in the semen of COVID-19 patients; this further supports the pyrexia hypothesis and the effects of cytokines released thereof [38]. Other potential mechanisms postulated include the viral entry portal of testicular receptors. The ACE2 and TMPRSS2 receptors in male reproductive tissues act as crucial gateways for SARS-CoV-2 entry into host cells [39, 40]. The entry of the virus and the consequent overtake of the protein synthetic mechanisms, particularly those for spermatogenesis, have resulted in lower gonadal function, as reported among COVID-19 patients [26]. This is expressed as a decreased serum LH to serum testosterone ratio among these patients and has corroborated findings among healthy controls. The findings of a marked decrease in serum testosterone, FSH, and LH levels with similar PRL levels in our COVID-19 patients further supports this postulation [41].

Although postmortem findings have reported drastic sperm cell damage and losses, which in turn query the reproductive capacity of SARS-CoV-2-infected men post-recovery [8], Hu et al. and Enikeev D et al.'s opposing reports of improved semen quality in recovered patients are promising [10, 35]. The presence of the virus in the semen of COVID-19 patients—an outcome that reinforced the need for reevaluation of the virus' impact on male reproduction—further supported the earlier submission [30]. Investigating the potential impact of COVID-19 on male fertility and its underlying mechanisms requires further research, particularly in comparison to the effects of other viral infections. With over 27 viruses reported to infect human semen and disrupt spermatogenesis, the possibility of SARS-CoV-2 inducing the same reproductive impairment with similar mechanisms has been explored with supporting findings [14]. Several factors, like the host immunity and the specific viral characteristics, contribute to the persistence of this genetic material in semen. The male reproductive system has an immunosuppressive environment that protects spermatozoa from potentially harmful immune responses. This is vital for maintaining the integrity of sperm and facilitating successful fertilization. Whether this immunosuppressive microenvironment protects viruses from immune surveillance remains unclear, and this knowledge is crucial to assessing potential risks to fertility [42].

The findings of this study are important for reproductive health, especially among those with a history of COVID-19 infection. The effect of the virus and implications on spontaneous conception, pregnancies, and outcomes of assisted reproductive technology (ART) are robust. Complications such as ovarian hyperstimulation syndrome (OHSS) and tubo-ovarian abscess have been reported in specific settings [43]. These findings were, however, not significant. In investigating the effect of SARS-CoV-2 on assisted reproduction, Mor H. et al. reported no significant causal relationship between the change in the live birth rate and the pregnancy loss rate, as ART during the COVID-19 pandemic was considered fair, safe, ethical, and medically appropriate [44]. According to Wang M et al., findings from in vitro fertilization (IVF) studies show that male SARS-CoV-2 infection might impair clinical outcomes with a decrease in blastocyst availability and formation, which further impacts embryonic development [45]. For women pregnant with SARS-CoV-2-infected semen, the risk for cross-infection and pregnancy complications are heightened as cases of preeclampsia, preterm birth, or stillbirth are common [46]. Severe cases exhibit even stronger associations with preeclampsia, preterm birth, gestational diabetes, and low birth weight when compared with milder cases of the virus [46]. In a few instances, vertical transmission has been observed, with 3.2% of neonates born to COVID-19-positive mothers testing positive [46]. Furthermore, pathological examinations of placentas from infected mothers revealed vascular malperfusion and a potential viral presence, although fetal transmission rates remained low [47]. Oxidative stress has been reported to not only cause cytokine release but also induce abortive apoptosis, and sperm DNA fragmentation [48]. The impact of the virus on sperm DNA has been widely documented. Falahieh FM et al. reported a higher sperm DNA fragmentation index (DFI) in semen samples, directly linked to SARS-CoV-2 infections [49]. Also, Mannur S. observed severe oligo-astheno-teratozoospermia and significant sperm DNA damage, including the absence of acrosomes and fragmented sperm heads, 43 days after recovery from acute infection [50]. This damage caused extensive embryo fragmentation and poor implantation. Additionally, sperm DNA damage results in fragmented paternal chromosomes, which are randomly distributed between the two sister cells during the first cell division [51]. These findings have significant implications for both natural (unassisted) and assisted reproduction.

Concerns initially indicated that the virus might be transmitted through semen, impacting female fertility and pregnancy outcomes. In response to the COVID-19 pandemic, fertility societies worldwide, including the American Society for Reproductive Medicine (ASRM), the European Society of Human Reproduction and Embryology (ESHRE), and the International Federation of Fertility Societies (IFFS), swiftly issued guidelines to navigate ART treatments [52, 53]. These guidelines, supported by dedicated COVID-19 working groups, aligned practices with evolving scientific evidence and local health recommendations while ensuring continuous support for patients and professionals. Although the risks associated with COVID-19 in pregnancy and ART remained uncertain, guidelines advised against initiating new treatments and recommended postponing embryo transfers and elective surgeries except for urgent cases like oncology-related fertility preservation. As the pandemic evolved, ART services gradually resumed following declining local infection rates and healthcare resource availability, with clinics implementing stringent safety measures such as virtual consultations, patient screening, and enhanced infection control protocols [52, 53]. Currently, research examining the effects of SARS-CoV-2 infection on ART treatment has yielded inconsistent findings [54]. Rashidi BH et al. reported that successful pregnancy rates with ART might not be significantly affected by a male partner's COVID-19 infection [43]. This finding is similar to the Italian cohort study that found no differences in implantation rate, miscarriage, or clinical pregnancy rates over 749 treatment cycles [55]. On the contrary, Mannur S et al. in their case study reported a failed incidence of IVF in a previously uninfected Indian male, who acquired the SARS-CoV-2 infection a few days after embryo freezing. Histological assessment revealed severely damaged sperm DNA with teratozoospermia, although slight semen quality improvements were noted 135 days after recovery [50]. Most studies reporting adverse outcomes in ART following SARS-CoV-2 infection have not specified whether the male or female partner was affected, often reporting outcomes where both partners were infected [7].

While short-term semen parameter changes have been observed in some individuals recovering from SARS-CoV-2 infection, the long-term consequences for fertility remain unclear. These mild, short-term alterations might potentially translate into difficulties with conception and pregnancy maintenance in the future [56]. Persistent oxidative stress and DNA damage in sperm can lead to chronic fertility issues in men, including reduced sperm quality and genetic abnormalities in offspring [49, 50]. To definitively assess this, well-designed cohort studies with long-term follow-up are necessary. Considering the oxidative stress the virus imposes on protein synthetic machinery, strategies to manage these stressors in COVID-19 recovery may help preserve male fertility [57, 58]. Comparisons of outcomes in infected and non-infected groups are currently being done in studies, and further research is necessary to draw definitive conclusions. A multidisciplinary collaboration between virologists, reproductive endocrinologists, and andrologists is crucial to optimizing and maintaining male reproductive function during the infection and post-recovery phases of SARS-CoV-2 infection. Incorporating assessments of male reproductive health parameters in vaccine safety studies can address concerns related to the impact of COVID-19 vaccines on male fertility.

Limitations

This review provides a comprehensive overview of the existing literature on the impact of SARS-CoV-2 on semen parameters and male fertility; however, limitations were noted. The evolving nature of the virus, with research findings still in the early experimental stages, limits the findings of this review as ongoing research efforts constantly generate new knowledge. The commonest limitation was the widespread use of limited sample size across studies, which may limit the generalisability of study findings. The diversity across study designs is also noteworthy as this heterogeneity may hinder the ability to assert the causal relationship between COVID-19, semen quality, and fertility outcomes. Also, across most studies, there were no baseline pre-COVID semen analysis results to make an effective comparison. Our review could not explain the absence of SARS-CoV-2 RNA in some semen samples from reported studies, necessitating further investigation. This ambiguity is notable, especially since viremic patients (e.g., HIV, Zika virus patients) have been known to shed viruses into semen [59]. Current hypotheses on variability across studies on the presence of SARS-CoV-2 RNA in semen, such as those by Holtmann et al., suggest that SARS-CoV-2 RNA disappears rapidly after infection [30]. They also report that the virus crosses the blood-testis barrier only during the acute infection phase, not after the 21-day convalescence period [30]. These findings are not corroborated across other studies and currently limit our understanding of these reported variances. Studies on pregnancy outcomes by ART reported findings from co-infected couples, limiting the generalizability of pregnancy outcomes from SARS-CoV-2-infected semen. The review did not comprehensively explore the potential influence of comorbidities and lifestyle factors such as smoking or alcohol consumption on semen quality. A more holistic understanding of these factors is crucial for informing clinical decision-making regarding male fertility and COVID-19. Some studies reviewed identified viral RNA in semen; however, we could not make conclusions as the presence of the virus in semen may not necessarily translate to transmissible infectious virus particles.

Conclusion

SARS-CoV-2, the virus responsible for COVID-19, has adversely affected the global population, straining not only the healthcare system but nearly all spheres of life. Across the health sector, it continues to cause wide-ranging health outcomes that extend far beyond the respiratory system to others, including the male reproductive system. The current understanding of the potential impact of COVID-19 on male fertility and semen quality is complex and still evolving; however, most studies conducted have reported adverse outcomes with negative impacts on male reproductive potential. Supporting evidence of the presence of SARS-CoV-2 in semen and the consequent reduction in semen quality, including cellular damage and dysfunction, has been documented. Physiological complications and pathological outcomes include bilateral orchitis, ischemia-related priapism, and degenerated germ cells. While most studies have indicated potential alterations in semen parameters, testicular pathology, and hormone levels due to COVID-19, the long-term effects on male fertility biomarkers remain uncertain. A few studies have reported normal semen analysis and the absence of SARS-CoV-2 in semen studies post-recovery. The implications for assisted reproduction are promising, as fertility authorities have recommended the use of assisted reproductive technologies in the immediate post-pandemic era. Opposing trends underscore the need for long-term longitudinal follow-up studies to comprehensively assess reproductive outcomes years post-recovery by tracking semen quality and fertility outcomes in recovered individuals. A multidisciplinary management approach is advocated for optimal treatment outcomes and fertility potentials post-recovery. Collaboration with virologists and andrologists holds the potential for fertility preservation after SARS-CoV-2 infections.

Abbreviations

PHEIC	Public Health Emergency of Internation Concern
SARS-CoV-2	Severe acute respiratory syndrome coronavirus-2
ACE2	Angiotensin-converting enzyme-2
TMPRSS2	Transmembrane serine protease 2
CTD	C-terminal domain
DFI	DNA fragmentation index
IL-1β	Interleukin-1 beta
TNF	Tumor necrosis factor
IFNγ	Interferon-gamma
LH	Luteinizing hormone
FSH	Follicular stimulating hormone
PRL	Prolactin
TAC	Total antioxidant capacity
IVF	In vitro fertilization
ART	Assisted reproductive technology

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Authors' contributions
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