

REVIEW

Effects of coronavirus disease 19 (COVID-19) vaccination on male sexual function: a narrative review

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Abstract

Recent reports suggest that the coronavirus infectious disease (COVID-19) may negatively affect male sexual function. This evidence, together with the perplexity that has arisen in the population due to the need to vaccinate many people in a short time to face pandemic emergency, has also raised questions about the safety of COVID-19 vaccines regarding sexual function. The present narrative review aims to evaluate main evidence regarding the effects of vaccination on classical and advanced seminal parameters, erectile function, and sex hormones. Many studies supported by systematic reviews and meta-analyses have evaluated the impact of COVID-19 vaccination on sperm parameters and fertility, discovering no significant impact. The effects of vaccination on erectile function have been evaluated in only a few studies with some methodological limitations. However, no significant negative impact was found, and in one study, an improvement of sexual function following vaccination was actually observed. Regarding sex hormones, only a few sporadic cases of pituitary apoplexy and hypophysitis with involvement of the gonadal axis have been reported, which mainly occurred in patients with known pituitary lesions. The effects of COVID-19 vaccination on male sexual function appear minimal and of little clinical impact. Concerns that have arisen regarding the safety of the vaccine due to its rapid development in an emergency context, therefore, do not seem to be scientifically supported by the evidence that is currently available.

Keywords

Vaccine; SARS-CoV-2; COVID-19; Seminal parameters; Erectile function; Sex hormones; Fertility

Efectos de la vacunación contra la enfermedad por coronavirus 19 (COVID-19) en la función sexual masculina: una revisión narrativa

Resumen

Informes recientes sugieren que la enfermedad infecciosa por coronavirus (COVID-19) puede afectar negativamente a la función sexual masculina. Estas pruebas, junto con la perplejidad que ha surgido en la población debido a la necesidad de vacunar a muchas personas en poco tiempo para hacer frente a una emergencia pandémica, plantearon preguntas sobre la seguridad de las vacunas contra el COVID-19 también con respecto a la función sexual. La presente revisión narrativa tiene como objetivo evaluar las principales pruebas relativas a los efectos de la vacunación sobre los parámetros seminales clásicos y avanzados, la función eréctil y las hormonas sexuales. Muchos estudios respaldados por revisiones sistemáticas y metanálisis evaluaron el impacto de la vacunación COVID-19 sobre los parámetros espermáticos y la fertilidad sin descubrir ningún impacto significativo. Los efectos de la vacunación sobre la función eréctil se evaluaron en pocos estudios con algunas limitaciones metodológicas. Sin embargo, no se encontró ningún impacto negativo significativo, y en un estudio incluso se observó una mejora de la función sexual tras la vacunación. En cuanto a las hormonas sexuales, sólo se han descrito unos pocos casos esporádicos de apoplejía hipofisaria e hipofisitis con afectación del eje gonadal, que se produjeron principalmente en pacientes con lesiones hipofisarias conocidas. Los efectos de la vacunación COVID-19 sobre la función sexual masculina parecen mínimos y de escasa repercusión clínica. Por lo tanto, las preocupaciones que han surgido con respecto a la seguridad de la vacuna debido a su rápido desarrollo en un contexto de emergencia no parecen estar respaldadas científicamente por las pruebas disponibles.

Palabras Clave

Vacuna; SARS-CoV-2; COVID-19; Parámetros seminales; Función eréctil; Hormonas sexuales; Fertilidad

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of coronavirus disease 19 (COVID-19) that started in Wuhan, China, in December 2019, to become a pandemic causing a total of 778 million cases and 7 million deaths worldwide up to June 2025 [1].

Concerns about male sexual health and COVID-19 have arisen due to the binding of SARS-CoV-2 to the host cells which relies on an angiotensin-converting enzyme 2 (ACE-2), expressed by cells of several human tissues including the testis, and the subsequent entry into the cells through the priming of the viral spike protein regulated by Transmembrane Serine Protease 2 (TMPRSS-2), whose expression is modulated by androgens [2]. In fact, the entrance of SARS-CoV-2 in Leydig and Sertoli cells of the testis was thought to potentially deteriorate steroidogenesis and spermatogenesis leading to fertility problems, hypogonadism, and erectile dysfunction [3]. Despite initial reports suggesting otherwise [4], most authors have reported that SARS-CoV-2 does not appear to be detectable in the semen of COVID-19-infected subjects [5]. However, a temporary alteration in testicular function, both in terms of spermatogenesis [6] and hormone production [7], has been demonstrated. Long term COVID has also been associated with erectile dysfunction mainly through vascular and psychological alterations [8, 9].

To face the pandemic, a number of vaccines were tested and marketed worldwide. From December 2020, with the emergency use authorization by the Food and Drug Administration (FDA), the first mRNA vaccines (BNT162b2 and mRNA-1273, by Pfizer-BioNTech and Moderna, respectively) to target the SARS-CoV-2 Spike protein became available. According to the initial clinical trials, the mRNA-based vaccines demonstrated 94–95% efficacy in preventing symptomatic COVID-19 after a two-dose immunization regimen, but with a significant decline in antibody levels after about 6 months, requiring booster doses to ensure effective and prolonged immune response [10]. The efficacy and safety of COVID-19 vaccines are supported by several articles [11] and confirmed by a recent meta-analysis of controlled and randomized clinical trials (RCTs), with the most common side effects being injection site discomfort, fever, fatigue, and headache (54.5% of subjects) [12]. Nonetheless, attitudes toward COVID-19 vaccines varied greatly among the population, with hesitancy and opposition mainly due to safety concerns and a perceived lack of effectiveness, as well as a distrust of vaccine manufacturers and public health authorities [11]. The hesitation and mistrust towards vaccination was not only evident in the less educated population [13], but also in a certain section of people belonging to the health sector [14, 15]. According to the latest World Health Organization (WHO) reports, 13.64 billion vaccine doses have been administered worldwide so far, with 67% of the global population completing the primary vaccination series and 32% receiving at least one booster dose up to 31 December 2023 [1].

Among the health concerns related to mass vaccination, the effects on fertility were found to be particularly important, especially in the younger population. For example, misinformation on social media led young women to think that

COVID-19 vaccines could cause sterility [16]. In an on-line survey of 914 unvaccinated U.S. subjects (about half of whom were male), Diaz *et al.* [17] reported that 41% of subjects responded “Yes” and 38% “Unsure” to the question “Do you believe COVID-19 vaccines can negatively impact fertility and/or reproductive health”, identifying fertility as the main concern for vaccine hesitancy in this category of population.

The present narrative review, therefore, aims to discuss the available evidence on the possible effect of COVID-19 vaccines on male sexual function, to provide an objective view of the topic and highlight areas of criticality in our current knowledge.

2. Methods

A narrative review was conducted through an extensive search for literature on PubMed between February and June 2025. The following research terms were used in various combinations: “Vaccines”, “COVID-19”, “SARS-CoV-2”, “fertility”, “semen parameters”, “sperm parameters”, “advanced semen parameters”, “advanced sperm parameters”, “erectile dysfunction”, “testosterone”, “hypogonadism”, “sex hormones”. Papers were considered eligible if their topic was the effects of COVID-19 and/or COVID-19 vaccination on male fertility, classic semen parameters, advanced semen parameters, erectile function and/or testosterone levels. The following criteria were used for exclusion: animal studies and scientific articles not published in English. Three reviewers (AC, NdM and GS) independently evaluated the title, abstract, and full text of each potentially relevant manuscript for eligibility. Any discrepancies were resolved by discussion.

3. COVID-19 vaccination and classic seminal parameters

In the early phase of the pandemic emergency, the observation that SARS-CoV-2 was detectable in semen of COVID-19 infected subjects [4] suggested a tropism of COVID-19 for the testis with a possible direct contact between the virus and the germ cell during the infection. However, these findings were not confirmed in subsequent studies [18–21] even if many studies reported alterations in seminal parameters after COVID-19, probably resulting from the inflammatory context favoured by the infectious event [6, 22, 23]. In further support of this hypothesis, more significant alterations in seminal parameters were found in patients who developed a fever following infection than in asymptomatic patients [24].

Considering the negative effects of COVID-19 on spermatogenic function, concerns arose also regarding the possible effects of COVID-19 vaccination on male fertility. These were added to the worries of the public opinion on the safety of the vaccine, which had been developed in an emergency setting with reduced timelines compared with what is required in regular trials [25]. Many studies evaluated the effects of COVID-19 vaccination on spermatogenesis mainly considering sperm parameters as a surrogate marker of male fertility (Table 1, Ref. [26–31]). The majority of papers did not show significant negative effects of the vaccine on semen parameters [32–40]. In particular, in the study by Dong *et al.* [37], four groups of

TABLE 1. Summary of main studies evaluating classic seminal parameters.

Authors [Ref.]	Year	Sample Size	Study Design	Vaccine Type(s)	Outcomes	Main Findings
Huang <i>et al.</i> [26]	2023	914 males	Meta-analysis of 12 cohort studies	Inactivated (CoronaVac, BBIBP-CorV), mRNA (BNT162b2, mRNA-1273), viral- vector (Sputnik V, ChAdOx1 nCoV-19, Ad26.COV2.S) and heterologous (mRNA + viral vector, research codes not specified) vaccines	Semen volume, sperm concentration, sperm motility, sperm morphology, total sperm count	No significant differences between vaccinated and unvaccinated groups.
Zaçe <i>et al.</i> [27]	2022	1762 males	Meta-analysis of 14 before-after and 15 cohort studies	Inactivated (CoronaVac), mRNA (BNT162b2, mRNA-1273), viral-vector (Sputnik V) and heterologous vaccines (mRNA + viral vector, research codes not specified)	Sperm concentration, volume, motility, <i>in vitro</i> fertilization rates	No significant differences found in sperm concentration, volume, and motility. Vaccine type did not influence outcomes. No significant differences in biochemical parameters and clinical pregnancy rates.
Ma <i>et al.</i> [28]	2023	1674 males for total sperm motility, 920 for semen volume and sperm concentration, 1110 for total sperm count and 332 for morphological changes	Systematic review and meta-analysis of 7 before-after and cohort studies	Inactivated (research codes not specified) and mRNA vaccines (BNT162b2, mRNA-1273)	Total sperm motility, semen volume, sperm concentration, morphology, total sperm count	No significant differences in semen parameters between groups.
Li <i>et al.</i> [29]	2023	2498 males	Systematic review of 24 cross sectional or cohort studies	Inactivated (CoronaVac, BBIBP CorV), mRNA (BNT162b2, mRNA-1273), viral-vector (Sputnik V) and heterologous vaccines (mixed formulations not specified)	Total sperm count, sperm concentration, sperm morphology, progressive motility, total motile sperm count	No significant alterations found in semen parameters post-vaccination.
Wang <i>et al.</i> [30]	2024	6007 males	Retrospective study on IVF patients	Virus-vector, recombinant subunit, and inactivated vaccines (research codes not specified)	Clinical pregnancy rates, semen parameters	No significant differences in IVF outcomes or semen parameters based on vaccination status.
Dong <i>et al.</i> [31]	2024	409 males	Retrospective cohort study	Inactivated SARS-CoV-2 vaccines (research codes not specified)	Sperm volume, total motility, progressive motility, concentration, morphology, and sex hormone levels	Significant decrease in total sperm motility post-vaccination (46.90% vs. 58.62%), but within normal range. Other semen parameters unaffected.

IVF: *In Vitro* fertilisation; SARS-CoV-2: *Severe acute respiratory syndrome coronavirus 2*.

patients were evaluated: 168 unvaccinated, 8 one-dose vaccinated, 183 fully vaccinated, and 160 vaccinated with booster dose. No significant difference in classic seminal parameters was found between the vaccinated and unvaccinated groups [37]. Similarly, in the study by Huang *et al.* [38], semen parameters measured before and after inactivated SARS-CoV-2 vaccination in 128 men did not show any significant difference. In contrast, some studies reported a negative effect of vaccines on semen parameters. Indeed, Gat *et al.* [41] conducted a study on 37 sperm donors and found a decrease in sperm concentration and total motility count (TMC) 3 months after COVID-19 vaccination with BNT162b2, but a full recovery was then observed in subsequent follow up evaluations. Abd *et al.* [42] described a statistically significant reduction in total sperm motility and progressive motility after vaccination, but these parameters remained within the normal range. Taken together, these data seem to suggest that the observed sperm quality impairment was transitory and not clinically relevant.

Despite the evidence leaning more towards the absence of a negative effect of vaccination on male fertility, the global impact of the issue has led to copious literature being examined and synthesised by multiple systematic-reviews and meta-analyses. In 2022, a meta-analysis of Huang *et al.* [26] evaluated twelve cohort studies and involved a total of 914 participants. The vaccinated subjects did not show any significant differences regarding semen volume, sperm concentration, total sperm motility, progressive sperm motility, total sperm count, total motile sperm count, total progressively motile sperm count, and sperm morphology in comparison with the unvaccinated group [26]. In the same year, a meta-analysis by Zaçe *et al.* [27] evaluated 29 studies (14 pre-post vaccination studies and 15 cohort studies) to evaluate the effects of the vaccine on sperm quality and fertility rates in women who underwent *in vitro* fertilisation (IVF). Fifteen studies were conducted on females, 11 on males, and 3 on both components of a couple. No significant differences were found regarding sperm concentration, volume, and motility. The effects on semen parameters were not influenced by the type of vaccine used. Biochemical and clinical pregnancy rates did not show any significant differences between the vaccinated and unvaccinated groups [27]. In 2023, Ma *et al.* [28] conducted another systematic review and meta-analysis. Once again, no significant differences were found regarding total sperm motility, semen volume, sperm concentration, morphological change, and total sperm count in the pre- and post-vaccination studies analysed. Inactivated or messenger RNA (mRNA) COVID-19 vaccinations did not show any different effects on semen parameters [28]. In addition, a systematic review by Li *et al.* [29] reported data from 24 pre- and post-vaccination cohort studies respectively on: males affected by infertility undergoing assisted reproduction techniques (ART), healthy volunteer sperm donors, and males affected by type 2 diabetes without other relevant diseases. The included studies reported different sperm parameters: 9 evaluated total sperm count, 23 evaluated sperm concentration, 7 evaluated sperm morphology, 19 evaluated total sperm motility, 17 evaluated progressive sperm motility, and 11 evaluated total motile sperm count (TMSC). The results of this systematic review confirmed the absence of significant alterations in semen parameters after

vaccination [29].

Regarding the most recent evidence, a large retrospective study on 6007 couples undergoing IVF evaluated clinical pregnancy rates and semen parameters according to the vaccination status of males, females, and couples (vaccinated male with unvaccinated female, unvaccinated male with vaccinated female, both male and female vaccinated or both male and females unvaccinated). Among the different group of patients, no significant differences were found in IVF outcomes and semen quality [30]. In another retrospective cohort study, by Dong *et al.* [31], 409 males without previous SARS-CoV-2 infection showed a significant decrease in total sperm motility after vaccine administration ($46.90 \pm 2.40\%$ vs. $58.62 \pm 2.51\%$; $p = 0.001$). However, the parameter remained within the normal range, and all the other main semen parameters (volume, sperm concentration, total sperm count, progressive motility and normal forms) were not affected by significant modifications [31].

In conclusion, the evidence available does not support a negative effect of COVID-19 vaccines on semen quality and fertility rates of couples undergoing IVF. Notably, a significant limitation of the described studies is the definition of vaccine status mainly based on self-reports and the short follow-up period. Data from large longitudinal studies with adequate follow-up time could, therefore, add information in the future. However, a negative impact on fertility and semen parameters in subsequent months following the vaccination seems unlikely, considering that the scarcely significant alterations found in only a few cases were frequently resolved within the first few months following vaccination.

4. COVID-19 vaccination and advanced seminal parameters

Classic seminal parameters can provide important information in the assessment of an infertile subject, but there are clinical situations where data provided by these parameters may not be sufficient. In particular, in cases of unexplained infertility, where infertility is associated with basal seminal parameters in the normal range, or idiopathic infertility, where impaired classic seminal parameters were found without a defined clinical reason, advanced seminal parameters may be a valuable addition [43]. Indeed, these parameters provide useful information about sperm DNA integrity, chromatin status, anti-sperm antibodies, levels of reactive oxygen species (ROS), and the presence of inflammatory or pro-inflammatory factors. For example, they may be able to identify clinical situations where oxidative stress represents the predominant pathophysiological mechanism, leading to specific antioxidant treatments [44]. In fact, oxidative stress can impair fertility through alteration in classic semen parameters, but also damaging sperm membranes and DNA, leading to difficulties in the interaction between spermatozoa and egg even in the presence of normal classic semen parameters [45].

Current data on the effects of SARS-CoV-2 vaccines on advanced seminal parameters are limited (Table 2, Ref. [28, 46–50]). As an inflammatory disease, COVID-19 infection could increase oxidative stress, impairing both classical and advanced seminal parameters [2]. A commonly accepted hy-

TABLE 2. Summary of main studies evaluating advanced seminal parameters.

Authors [Ref.]	Year	Sample Size	Study Design	Vaccine Type(s)	Outcomes	Main Findings
Olana <i>et al.</i> [28]	2022	47 males	Prospective cohort study	mRNA vaccine (BNT162b2)	Basic semen analysis, Seminal electrolyte levels, IL-6, reactive oxygen metabolites	No significant differences detected in seminal parameters post-vaccination.
Chatzimel <i>et al.</i> [50]	2022	1 male	Case report	mRNA vaccine (research codes not specified)	Basic semen analysis, DFI	After three doses of mRNA vaccine, sperm concentration increased; motility, morphology, and DFI remained stable.
Lestari <i>et al.</i> [49]	2023	70 infertile males	Cross-sectional study	mRNA (mRNA-1273), inactivated viral (CoronaVac), viral vector (ChAdOx1 nCoV-19) vaccines	Basic semen analysis, DFI	Men vaccinated with viral vector vaccine exhibited a significant increase in DFI compared to other vaccine types.
Murata <i>et al.</i> [46]	2022	4 cases	Case report	mRNA vaccine (BNT162b2)	Cytokine levels, semen quality	Cytokine storm observed, suggesting an immune disruption of spermatogenesis.
Schaler <i>et al.</i> [47]	2024	17 normozoospermic males	Longitudinal cohort study	Recombinant vaccines (Ad26-COV2 DNA, BNT162b2 mRNA)	Inflammatory markers, seminal plasma	Vaccination led to temporary increases in systemic and seminal inflammation, affecting sperm parameters.
Zhao <i>et al.</i> [48]	2024	1639 males	Retrospective cohort study	Inactivated vaccines (CoronaVac, BBIBP-CorV, KCONVAC), recombinant protein vaccine, inactivated and recombinant protein vaccines (Sinovac/BBIBP-CorV/ZF2001), viral vector vaccines (Ad5-nCoV), inactivated and mRNA vaccines (Sinovac/BBIBP-CorV/BNT162b2)	Basic semen analysis, leukocytes analysis, DNA fragmentation, antisperm antibodies	Inactivated vaccines led to quicker recovery of sperm quality compared to recombinant protein vaccines, with a temporary rise in DNA fragmentation.

DFI: DNA fragmentation index; IL-6: Interleukin-6.

pothesis also suggests that vaccines may trigger an immune response that could temporarily disrupt spermatogenesis, potentially causing short-term declines in sperm quality, particularly when accompanied by a fever [35, 46]. This evidence was supported by a longitudinal cohort study conducted on 17 normozoospermic men who experienced changes in seminal parameters during both the acute post-vaccination phase (24–72 hours) and three months after the vaccination. While no significant changes in DNA integrity were observed, transient increases in monocyte chemoattractant protein-1 (MCP-1) and interleukin-8 (IL-8) levels in seminal plasma were detected,

suggesting a brief activation of the immune system that could also affect the testes [47]. Likewise, a transient decline in sperm quality, particularly following COVID-19 infection, was suggested by Zhao *et al.* [48], who retrospectively investigated the effects of different COVID-19 vaccines (inactivated vaccines or recombinant protein vaccines) in a large cohort of men in China. They included 1639 vaccinated men who were subdivided, based on previous COVID-19 infection, into uninfected and previously infected (the latter subdivided by time of recovery from COVID-19 into less than 30 days, 30–90 days, and more than 90 days). 85.2% of the participants had

suffered from COVID-19. Temporary but reversible increase in sperm DNA fragmentation index (DFI) and high DNA stainability (HDS), along with a rise in antisperm antibodies, was observed, particularly during the acute phase of infection (within 30 days), but all the observed changes disappeared over time from recovery. Notably, receiving two doses of an inactivated vaccine appeared to offer less protection to sperm quality compared to recombinant protein vaccine boosters [48]. An interesting study by Lestari *et al.* [49] examined the sperm DFI in 70 infertile men, comparing those who had been infected with COVID-19, those who had not, and those vaccinated with mRNA, inactivated viral, or viral vector vaccines. The men receiving the vaccination had not been previously affected by SARS-CoV-2. Interestingly, the men vaccinated with the viral vector vaccine exhibited a significant increase in DFI compared with those who received other vaccine types or men who were neither infected with SARS-CoV-2 nor vaccinated. However, the authors could not confirm the outcomes due to the lack of a further follow-up [49].

However, not all the studies suggested an adverse effect of COVID-19 vaccination on semen quality. In a case report by Chatzimeletiou *et al.* [50], the administration of three doses of an mRNA COVID-19 vaccine, combined with treatments for Ankylosing Spondylitis, was associated with an increase in sperm concentration, while motility, morphology, and DFI remained stable, suggesting no negative impact on sperm quality [50]. Similarly, Olana *et al.* [28] focused on the effects of the BNT162b2 mRNA COVID-19 vaccine on sperm parameters of 47 men, before and three months following vaccination, and no significant differences were detected in seminal electrolyte levels, interleukin-6 (IL-6) concentrations, or reactive oxygen metabolites [28]. Moreover, regarding DNA integrity and sperm chromatin condensation, no significant effects were observed when comparing the actions of different vaccine types [41].

In conclusion, while studies indicate that SARS-CoV-2 vaccination might cause temporary changes in some seminal parameters, such as DFI and chromatin condensation, these effects don't seem to be significant or long-lasting. Differences found in sperm quality alterations among different types of vaccinations are interesting but difficult to explain. In fact, confounding factors, such as post vaccination fever, that could influence these parameters are not easy to evaluate. Overall, sperm quality tends to return to normal over time. However, more research is needed to confirm these results and to explore any potential long-term impacts.

5. COVID-19 vaccination and erectile function

In recent years, a correlation between COVID-19 and erectile dysfunction (ED) has been highlighted. Specifically, it has been observed that in the clinical context of "Long COVID", multiple pathophysiological mechanisms can alter erectile function. This condition can in fact be associated with endothelial dysfunction, altered pulmonary function up to pulmonary fibrosis and alterations in the psychiatric sphere, such as anxiety and depression. These factors collectively contribute to vascular and psychological impairments that

can affect erectile function [8, 9]. Considering this evidence, concerns have arisen about the possible negative effects of COVID-19 vaccination on sexual function. However, to date few studies have assessed the impact of COVID-19 vaccination on erectile function (Table 3, Ref. [51–53]).

Mehta *et al.* [51] evaluated the impact of vaccination on 465 sexually active Indian males aged between 20 and 50 years. The International Index of Erectile Function 15 (IIEF15) questionnaire was administered with an addition of 15 questions to evaluate general sexual function and the specific impact of COVID-19 vaccination on each sexual domain (erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction). 71% of the patients reported no impact, 3% a decline, 2.7% an improvement, and 23.3% could not assess the impact of vaccination on sexual function. No differences, in terms of age, were found among the groups. Information regarding the type of vaccination administered was not reported; however, it is worthy to note that in the early phase of COVID-19 vaccination in India, 90% of the people vaccinated received Covishield ChAdOx1-S and 10% Covaxin BBV152. According to their results, the authors concluded that COVID-19 vaccination did not seem related to a significant adverse impact on male sexual function [51].

Similarly, Diaz *et al.* [52] conducted a survey on US males to evaluate the impact of COVID-19 vaccination on erectile function. 138 adult males were included, 121 vaccinated and 17 unvaccinated, according to the following criteria: age ≥ 45 years old and with no history of ED diagnosis. An anonymous 16-question survey, including the International Index of Erectile Function 5 (IIEF-5), was administered. The median IIEF-5 score among those vaccinated was 20, compared to 22 in the unvaccinated group. This finding was not statistically significant and cohort size differences had an important role, since 87.7% of patients were vaccinated. In conclusion, this survey showed no association between COVID-19 vaccination and new diagnosis of ED in males older than 45 years [52].

Başer *et al.* [53] conducted another online survey among healthcare professionals in Turkey. The survey included sexually active healthcare professionals having at least weekly intercourse, aged ≥ 18 years, who had received a complete immunization schedule. Exclusion criteria were a history of pelvic surgery or radiotherapy and psychiatric disorders. All the participants had to complete a questionnaire including the IIEF15, the Arizona Sexual Experiences Scale (ASEX) and the Beck anxiety inventory (BAI). A total of 170 participants were included. This study found an improvement, comparing pre- and post-vaccination, in IIEF, ASEX, and BAI scores and a statistically significant increase in the duration of sexual intercourse, showing positive changes in sexual functions after vaccination [53]. In conclusion, the evidence available does not suggest a negative effect of COVID-19 vaccination on sexual function. On the contrary, vaccination seems to play a protective role by mitigating the vascular and psychological consequences of COVID-19 infection.

In fact, in the study by Başer *et al.* [53] the administration of COVID-19 vaccines seems to ameliorate the quality of intercourse. These results are not surprising, since the link between COVID-19 and ED is well-established, and the COVID-19 vaccine administration could prevent or mitigate some of the

TABLE 3. Summary of studies evaluating erectile function.

Authors [Ref.]	Year	Sample Size	Study Design	Vaccine Type(s)	Parameters Assessed	Main Findings
Mehta <i>et al.</i> [51]	2023	465	Cross-sectional survey	Viral-vector (ChAdOx1-S, BBV152) vaccines	Erectile function (IIEF15)	71% reported no impact, 3% a decline, 2.7% an improvement, and 23.3% could not assess the impact of vaccination. No significant adverse effects on male sexual function.
Diaz <i>et al.</i> [52]	2022	138	Cross-sectional survey	mRNA (BTN162b2, mRNA 1273) and recombinant protein (Jcovden) vaccines	Erectile function (IIEF-5)	No statistically significant association between COVID-19 vaccination and erectile dysfunction.
Başer <i>et al.</i> [53]	2023	170	Cross-sectional survey	mRNA (BTN162b2), inactivated virus (CoronaVac) or heterologous (BTN162b2 + CoronaVac) vaccine	Erectile function (IIEF15), sexual experience (ASEX), anxiety (BAI)	Statistically significant improvements in sexual function, sexual experience, and anxiety after vaccination. Positive changes in sexual health.

IIEF: Internation Index of Erectile Function; ASEX: Arizona Sexual Experiences Scale; BAI: Beck Anxiety Inventory; COVID-19: coronavirus disease 19.

detrimental effects of SARS-CoV-2 infection. However, it must be considered that the little evidence available derives from studies with significant limitations. Indeed, the study by Başer *et al.* [53] presented a probable selection bias by analysing only healthcare professionals, potentially leading to better results by removing the psychological component of fear related to the lack of knowledge of the vaccine. Instead, in the study by Diaz *et al.* [52] the presence of a relevantly larger number of vaccinated patients in comparison to unvaccinated ones created important cohort size effects leading to difficulties in the statistical evaluation of results.

6. COVID-19 vaccination and sex hormones

An association between SARS-CoV-2 infection and low serum testosterone levels has been reported [54]. Indeed, as a systemic inflammatory disease, COVID-19 may cause suppression of gonadotropic secretion by the pituitary gland that leads to decreased testosterone production by the testes (*i.e.*, functional hypogonadism) [55]. In addition, COVID-19 may impair gonadotropin secretion through direct damage to the pituitary gland by causing hypophysitis or pituitary apoplexy [56, 57]. On the other hand, a possible direct effect of COVID-19 on testosterone testicular secretion has been suggested as well. That hypothesis is strengthened by the finding of a decline in testosterone levels in association with a rise in luteinizing hormone (LH), prolactin, and estradiol levels in a systematic review and meta-analysis of 2024 [7]. Despite the evidence concerning the effects of COVID-19 on gonadal function, few studies are available on the influence of COVID-19 vaccines on male hormones (Table 4, Ref. [42, 58–60]).

In 2024, a retrospective study evaluated 383 men with different vaccination status (unvaccinated, one dose, two doses or three doses of vaccine). Significantly higher levels of prolactin

and follicular stimulating hormones (FSH) were found in men who received only one vaccine in comparison with the others, but the authors highlighted that the small sample size (only 11 patients were included in this group) could have conditioned their observation. Nonetheless, the total testosterone and LH levels showed no significant differences among the four groups [42].

Alteration in gonadotropin production has been described in association with specific pituitary disorders. Aliberti *et al.* [58] described a case of pituitary macroadenoma apoplexy, with the patient suffering from adrenal insufficiency and asymptomatic hypogonadotropic hypogonadism the day after his third dose of SARS-CoV-2 vaccine. The patient underwent tumor transphenoidal resection and the pathology report showed pituitary adenoma with focal hemorrhage and necrosis. Interestingly, immunohistochemical evidence of SARS-CoV-2 proteins next to the pituitary capillaries suggested a previous exposure to SARS-CoV-2 as a contributing factor. The alterations described were transient considering that at the 4-month follow-up, a complete recovery of glucocorticoid and gonadotropic axis was observed, but the authors warned about the risk of pituitary apoplexy after vaccine in individuals with previous SARS-CoV-2 infection [58].

Hypophysitis after COVID-19 vaccination, with different clinical and biochemical manifestations, was also described. In a first case report, a 51-year-old man was suffering from headache, nausea, vomiting, malaise, and arthralgias a few days after the second dose of mRNA-1273 vaccination. Biochemical evaluations showed deficits of adrenal, thyrotropic, and gonadotropic axis, the latter associated with symptoms of hypogonadism, such as ED and decreased libido. The brain magnetic resonance imaging (MRI) was suggestive of hypophysitis, and during the follow-up, a spontaneous normalization of gonadotropic function was observed [59]. In another

TABLE 4. Summary of studies evaluating sex hormones.

Authors [Ref.]	Year	Sample Size	Study Design	Vaccine Type(s)	Parameters Assessed	Main Findings
Dong <i>et al.</i> [42]	2024	383 males	Retrospective cohort study	Inactivated vaccine (research codes not specified)	Prolactin, FSH, Testosterone, LH, E2, and T/LH ratio	Higher levels of prolactin and FSH in males who received only one vaccine dose compared to other groups. No significant differences in testosterone, LH and E2 levels.
Aliberti <i>et al.</i> [58]	2022	1	Case report	mRNA (BNT162b2 (1 dose) + mRNA 1273 (3 doses)) vaccines	Testosterone, LH, Cortisol, TSH, fT4, FSH, PRL	Pituitary apoplexy and adrenal insufficiency after third vaccine dose. Complete recovery of gonadotropic axis at 4-month follow-up.
Murvelashvili & Tessnow [59]	2021	1	Case report	mRNA (mRNA-1273) vaccine	Testosterone, FSH, LH, Cortisol, TSH, fT4, ACTH, PRL	Hypophysitis after second vaccine dose with symptoms of erectile dysfunction and decreased libido. Gonadotropic function normalized during follow-up.
Yu <i>et al.</i> [60]	2024	1	Case report	Non-specified	Testosterone, FSH, LH, Cortisol, TSH, fT3, T3, T4, ACTH, PRL	Hypophysitis after second vaccine dose in a patient with Rathke's cleft cyst. Symptoms of hypogonadism developed one year later.

FSH: Follicular Stimulating Hormone; LH: Luteinizing Hormone; E2: Estradiol; TSH: Thyroid-stimulating hormone; ACTH: Adrenocorticotrophic hormone; PRL: prolactin; fT3: free triiodothyronine; fT4: free thyroxine; T3: triiodothyronine; T4: thyroxine.

case report, a 59-year-old man with a history of Rathke's cleft cyst was suffering from hypophysitis associated with a deficit of all pituitary tropins, but with normal testosterone levels after the second dose of non-specified COVID-19 vaccination. After one year of follow-up, symptoms of hypogonadism were reported, and hypogonadotropic hypogonadism was diagnosed [60]. Interestingly, the manifestations described occurred during the second or third vaccine doses, but not after the first one. We do not have enough data to evaluate if specific types of vaccines are associated with a major risk. The hypogonadotropic hypogonadism seems to be reversible in most cases [58, 59], but in one patient, it was diagnosed one year after the vaccination and remained permanent [60]. Also, clinical manifestations of hypogonadism seem to be variable and not described in all cases of hypogonadotropic hypogonadism [58–60]. Interestingly, pre-existing expansive pituitary lesions (macroadenoma or Rathke's pouch cyst) were described in most cases [58, 60]; no relevant systemic diseases, no known coagulation disorders or autoimmune diseases were mentioned [58, 60]. Two main pathogenetic mechanisms were suggested: vaccine-induced thrombophilia-thrombocytopenia (VITT) syndrome or autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA) [58]. It has been assumed that these two mechanisms occur more easily when the pituitary gland is abnormal and therefore “fragile”, as in the cases of expansive lesions [61]. It is worthy to note that Aliberti L. *et al.* [58] described the detection of the virus in the tissue of the resected macroadenoma and hypothesized that the patient previously had an asymptomatic COVID-19 infection, and that the vaccination triggered a cross-reaction resulting in bleeding at the pituitary level [58].

7. Conclusions

The evidence available clearly points to the absence of a clinically relevant effect of COVID-19 vaccination on semen parameters and male fertility, confirming the excessive concern raised in public opinion and fostered in part by misinformation on the topic. Regarding erectile function, even if only a few studies with important methodological limitations are available, a negative effect of vaccination seems to be unlikely. In addition, the negative effects of COVID-19 on erectile function derive from the virus' biological activity which is not present in the vaccine, and therefore these negative effects should also be prevented. The more relevant findings regard some cases of pituitary apoplexy and hypophysitis with involvement of the gonadal axis. However, it should be noted that these events were particularly rare and occurred mainly in patients with known pituitary lesions. Finally, there is a lack of randomized controlled trials specifically focused on the effects of COVID-19 vaccines and male fertility.

AVAILABILITY OF DATA AND MATERIALS

No new data were created or analyzed in this study. Data sharing is not applicable to this article.

AUTHOR CONTRIBUTIONS

AC, GS, and NdM—designed the research study and performed the research. AC, GS, NdM, NA, MP, SR, SS—wrote the manuscript. GB—supervised the work and provided

important methodological insights. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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