Original Article

A comparative study of the effects of the COVID-19 pandemic on semen quality based on a nationwide relaxation of COVID-19 restrictions in China at the end of 2022

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Background: An association between the coronavirus disease 2019 (COVID-19) and a reduction in male semen parameters has been described, but no large-scale population analyses have been conducted. This study aimed to investigate the effects of the COVID-19 pandemic on semen quality. Based on a large-scale ecological comparative study, our study analyzed the impact of the COVID-19 pandemic on semen quality after the national liberalization of restrictions in China at the end of 2022, aiming to explore the impact of the COVID-19 pandemic on semen quality, and provide a basis for the study of the impact of subsequent epidemics on male reproduction as well as clinical diagnosis and treatment.

Methods: It is a population-based cross-sectional study. This comparative study was based on the nationwide loosening of COVID-19 curbs in China on December 7, 2022, 1 month after which, an 89% infection rate was reported in Henan Province, China. We compared semen quality and serum hormone levels from January 7, 2023 to April 30, 2023 and January 7, 2022 to April 30, 2022 at the Reproductive Center of Henan Provincial People's Hospital.

Results: Our results indicated a significant decrease in semen volume, sperm concentration, total sperm count, progressive sperm motility rate, and non-progressive sperm motility rate following the nationwide relaxation of COVID-19 restrictions. The effects on the semen volume and total sperm count persisted over time. Additionally, an increase in the incidence of sperm neck defects has been reported. Infection also led to hormonal disruptions, including alterations in prolactin (PRL), testosterone (T), sex hormone-binding globulin (SHBG), and the free testosterone index (FTI) along with an increase in osteocalcin and 25-hydroxy vitamin D (25-OH-VD).

Conclusions: The present study revealed that mild COVID-19 appears to have a detrimental effect on semen quality.

Keywords: Semen quality; coronavirus disease 2019 (COVID-19); sperm; hormones; mild

Submitted Oct 10, 2024. Accepted for publication Feb 10, 2025. Published online Mar 26, 2025.
doi: 10.21037/tau-24-562
View this article at: https://dx.doi.org/10.21037/tau-24-562

Introduction

Over the past four decades, a significant decline in sperm production, characterized by an annual 1.6% decrease in sperm count and a potential global decline in semen quality was observed (1). The impact of lifestyle factors-including alcohol consumption, smoking, psychological stress, obesity, exposure to endocrine disruptors, mobile phone usage (2,3), and infections (4) on semen quality has been extensively discussed. Recently, the decline in semen quality associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has emerged as a prominent topic of interest owing to the global pandemic (5,6).

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, was declared a pandemic by the World Health Organization on March 11, 2020. As of July 2023, more than 671 million cases have been documented worldwide, resulting in over 6.77 million deaths. Both severe (7) and moderate (5) COVID-19 are associated with a significant reduction in total and progressive sperm motility. A recent meta-analysis indicated that men who recovered from COVID-19 exhibited reduced sperm concentration and total sperm count and normal sperm morphology (8). Conversely, other studies suggest that mild COVID-19 does not adversely affect semen quality (9,10). Thus, the effect of mild COVID-19 on semen quality remains a subject of ongoing debate.

Compared to the effects on semen quality, the impact of COVID-19 on male sex hormones remains ambiguous, with limited studies exploring this relationship. One study involving 88 participants (44 controls and 44 cases) reported increased luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels in patients with severe symptoms (7). A recent meta-analysis indicated that COVID-19 is associated with decreased testosterone (T) and increased LH levels (5). Conversely, another recent meta-analysis found no significant differences in sex-related hormone levels before and after infection in patients with mild or no symptoms (8).

Previous studies focusing on clinical or rehabilitation patients have often been limited by small sample sizes, with meta-analyses involving pooled subjects with fewer than three thousand individuals. During the initial stages of the COVID-19 epidemic, many countries implemented social distancing and lockdown policies to curb the spread of the virus. China's zero-COVID policy was proved highly effective, resulting in significantly fewer cases than other nations with much smaller populations, recording only 367,627 confirmed symptomatic cases and 5,235 deaths as of December 13, 2022 (https://www.china-briefing.com/news/living-with-covid-what-does-the-pivot-mean-for-businesses-in-china/). On December 7, 2022, the National Health Commission announced a set of 10 measures that effectively dismantled China's zero-COVID strategy, eliminating the requirements for mandatory centralized quarantine, compulsory testing, and extensive lockdowns. A month after the nationwide relaxation of COVID-19 restrictions, Henan Province reported an infection rate of 89% (https://www.henan.gov.cn/2023/01-09/2669528.html). This transitional period in China's COVID-19 prevention and control policies has created a unique opportunity to study the impact of the virus on semen quality using a large sample size. A comparative study was conducted to assess semen quality parameters and serum hormone levels from January 7 to April 30, 2023 (pandemic patients) and from January 7 to April 30, 2022 (control group, isolated from COVID-bearers) at the Reproductive Center of Henan Provincial People's Hospital. At the end of 2022 and the beginning of 2023, the predominant strain in China was Omicron BA.5.2, which was generally associated with mild symptoms or asymptomatic cases. Our study used a large sample size to reveal the impact of COVID-19 on semen quality and provide a theoretical basis for future studies of potential mechanisms. We present this article in accordance with the STROBE reporting checklist (available

Highlight box

Key findings

- The mild coronavirus disease 2019 (COVID-19) appears to have a detrimental effect on semen quality.

What is known and what is new?

- An association between the COVID-19 and a reduction in male semen parameters has been described. However, no large-scale population analyses have been conducted.
- We compared semen quality and serum hormone levels from January 7, 2023 to April 30, 2023 and January 7, 2022 to April 30, 2022 at the Reproductive Center of Henan Provincial People's Hospital. Our findings revealed a reduction in semen quality and alterations in serum hormone levels after recovery from COVID-19 with mild symptoms.

What is the implication, and what should change now?

- It is worth noting that infection with COVID-19 may be one of the mechanisms of semen quality decline and sex hormone disturbance in infertile men.

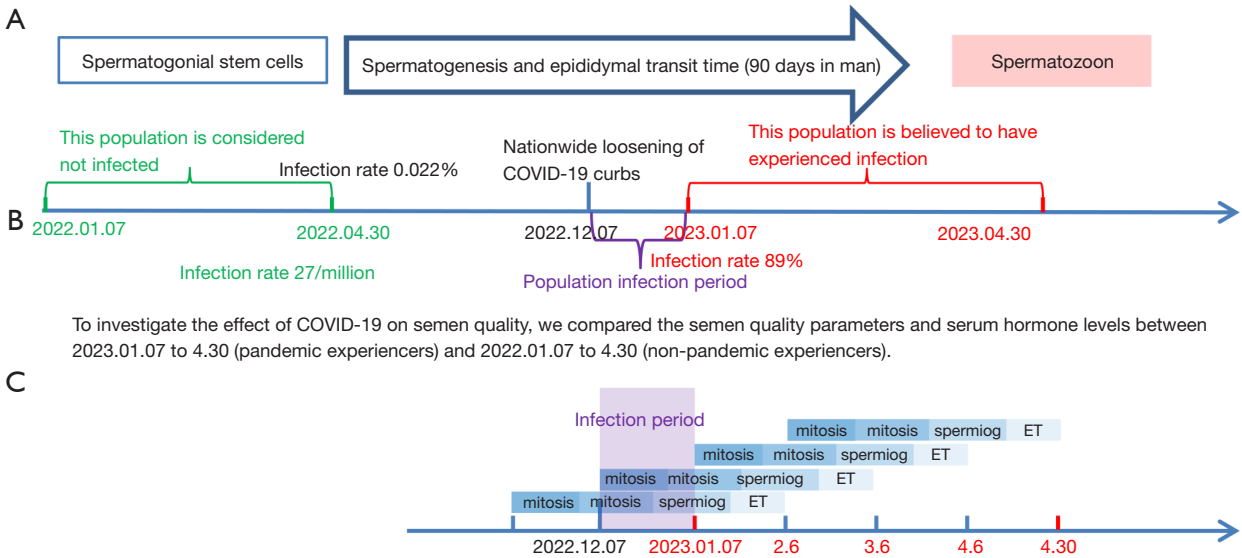

Figure 1 Study design and timeline of spermatogenesis exposed to COVID-19. (A) Spermatogenesis and ET last 90 days. (B) Timeline of government policy change and time selection of our study. (C) Correspondence of the observation date with duration of the spermatogenesis cycle and ET time. From 2023.01.07 to 03.06, the infection period overlapped the spermatogenic cycle, whereas from 2023.03.06 to 04.30, the infection period occurred before the spermatogenic cycle. COVID-19, coronavirus disease 2019; ET, epididymal transit.

at https://tau.amegroups.com/article/view/10.21037/tau-24-562/rc).

Methods

Study design and data collection

We conducted a comparative study focusing on a specific period of change in China's COVID-19 prevention and control policies. Our analysis compared semen quality parameters and serum hormone levels between two groups: individuals who experienced the pandemic from January 7 to April 30, 2023, and a control group from January 7 to April 30, 2022, sourced from the Reproductive Center of Henan Provincial People's Hospital. China's zero-COVID policy was in effect from January 23, 2020, to December 7, 2022. During this period, there were 2,695 reported infections, resulting in an infection rate of 27 per million as of April 29, 2022, in Henan Province (https://wsjkw.henan.gov.cn/2022/05-01/2442079.html). On December 7, 2022, the National Health Commission introduced a set of 10 measures that effectively dismantled the zero-COVID strategy, eliminating requirements such as mandatory centralized quarantine, compulsory testing, and widespread lockdowns. Prior to this data, there were 21,491 reported infections, leading to an infection rate of 0.02% in Henan Province (https://wsjkw.henan.gov.cn/2022/12-07/2652374.html). However, one month after the nationwide relaxation of COVID-19 restrictions, the infection rate in Henan Province surged to 89.0% on January 6, 2023, predominantly comprising patients with mild and asymptomatic infections, with the most prevalent strain identified as Omicron BA.5.2 (https://www.henan.gov.cn/2023/01-09/2669528.html). Therefore, the start date of our study was January 7. Given that the spermatogenic period spans three months, we conducted our observations on April 6. To assess the long-term effects, we extended the observation period by one month; however, owing to the May Day holiday, we were only able to collect data up to April 30. We divided the observation period into 4 months (January 7 to February 6; February 7 to March 6; March 7 to April 6; and April 7 to April 30) to evaluate both the short- and relatively long-term effects of infection, as well as the temporal dynamics following viral infection and the duration required for recovery. *Figure 1* shows the study design and the timeline of spermatogenesis in patients with COVID-19. Data from the Reproductive Center at Henan Provincial People's Hospital were collected from January 7, 2023, to April 30, 2023, and from January 7, 2022, to April 30, 2022, excluding cases of azoospermia. Data from the 2022 period served as controls. Participants who met all the

criteria were included; they were required to abstain for 2–7 days and were over 18 years of age. The exclusion criteria included a history of testicular injury, urologist-diagnosed inflammation of the urogenital system, epididymitis, treatment for varicocele, incomplete dislocation of the testis, or any of the following conditions identified by a urologist during physical examination: absence of a prominent areola, absence of pubic hair, abnormal breast development, absence of testis, abnormal penile structure, epididymal lumps, or varicocele. Data from the same period were selected to mitigate the effects of seasonal and temperature-related variations. Subjects visiting the reproductive center were considered to have recovered from COVID-19.

Measurement of semen parameters

Each subject abstained for 2–7 days. The semen parameters were analyzed using previously established methods (11,12). Semen volume was measured using the weighing method. Before providing a container to the client, the weight of the empty container was recorded. The container filled with semen was weighed and the weight of the container was subtracted from this measurement to calculate the volume of semen, assuming a semen density of 1 g/mL. Semen pH was measured using a precision pH paper. After thoroughly mixing the semen specimens, a drop of semen was evenly applied to the pH test paper (measuring range 6.0 to 10.0). The color of the impregnated area became uniform within 30 s and was compared with that of the standard strip. Computer-assisted sperm analysis (CASA) technology (Jiangsu Ruiqi Life Science Co., Ltd., Jiangsu, China, CFT-9201) was used to analyze semen samples. Following complete liquefaction of the semen, the specimen was thoroughly mixed, and a 10 µL aliquot was placed onto the sperm counting plate for analysis using an automatic semen analyzer. The evaluated indicators included complete liquefaction, semen volume, sperm concentration, progressive motility, nonprogressive motility, and overall sperm motility. The total sperm count was calculated by multiplying sperm concentration by semen volume. Sperm morphology was examined by staining. To prepare the semen smear, 1 mL of the semen sample was placed in a 10 mL plastic tube, followed by the addition of 5 mL saline. The solution was gently mixed and centrifuged at 800 ×g for 10 min. After centrifugation, the supernatant was discarded, 5 mL of normal saline was added and mixed, and the washing procedure was repeated. Subsequently, 10 µL of the suspension was placed on one end of a microscope slide using a pipette. The semen drops were dragged along the surface of the first slide at a 45-degree angle to the second slide, and the date and sample number were recorded. The smear was allowed to air-dry naturally and was subsequently stained using the Diff-Quik method. A total of 200 sperm cells were counted to assess the rates of normal morphology; abnormal morphology; teratozoospermia index (TZI); sperm deformity index (SDI); and head, neck, and tail defects. The microscope used for the CASA detection (Jiangsu Ruiqi Life Science Co., Ltd., CFT-9201) was operated by an inspection technician with professional qualifications. The standards for manual laboratory testing and semen quality were based on the WHO Laboratory Manual for the Examination and Handling of Human Semen (6th edition, 2021) (13).

Detection of serum sex hormones

Blood serum was used for hormone measurements. Fasting venous blood samples (5 mL) were collected from patients and subsequently centrifuged at 3,000 rpm for 10 min using a centrifuge with a radius of 10 cm to separate the serum. The analysis was conducted using a Roche e602 automatic electrochemiluminescence instrument (Cobas 8000 e 602, Basel, Switzerland) with appropriate supporting reagents. The levels of various hormones, including FSH, prolactin (PRL), LH, T, estradiol (E2), sex hormone-binding globulin (SHBG), free testosterone index (FTI), 25-hydroxy vitamin D (25-OH-VD), osteocalcin, and hydroxyprogesterone (OHP), were measured using the electrochemiluminescence method, strictly adhering to the kit's instructions. Elastase levels were determined using an automatic seminal plasma biochemical analyzer 2900 (Awareness Technology, Palm City, FL, USA). All semen parameters and hormone measurements were subjected to professional clinical training and quality control.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Xinxiang Medical University (09/15/2017; No. XYLL—20170311) and Medical Ethics Committee of Henan Provincial People's Hospital [(2021) Lunga No. (41)]. Informed consent was taken from all the patients.

Statistical analysis

SAS (version 9.4; SAS Institute) and R (version 4.3.0; R Development Core Team) were used for statistical

Table 1 Age distribution of the population

Date	2023 (pandemic experiencers)		2022 (the control)		*t*	P*
	N	Mean ± SD (years)	N	Mean ± SD (years)		
Jan. 07 to Feb. 06	847	31.85±5.21	372	32.54±4.90	–2.18	0.03*
Feb. 07 to Mar. 06	1,594	32.47±5.28	1,559	32.35±5.47	0.62	0.53
Mar. 07 to Apr. 06	1,542	32.99±5.54	1,346	32.65±5.60	1.64	0.10
Apr. 07 to Apr. 30	1,102	33.05±5.41	725	32.90±5.47	0.57	0.57
Jan. 07 to Apr. 30	5,085	32.65±5.39	4,002	32.57±5.47	0.70	0.48

We use a *t*-test to compare the differences in age between 2022 and 2023. *, P<0.05. SD, standard deviation.

analyses. We used the Kolmogorov-Smirnov test to assess the normality of the data and Levene's test to evaluate the homogeneity of variance. Age is reported as the mean ± standard deviation. Semen parameters, including semen volume, pH, sperm concentration, total sperm count, progressive sperm motility, non-progressive sperm motility, normal sperm morphology, and defects in the sperm head, neck, and tail are described as the median (Q1, Q3) owing to the skewed distribution of the variables. Serum hormone levels are expressed as medians (Q1 and Q3). The Wilcoxon two-sample test was used to compare the differences in semen parameters and serum hormone levels between 2022 and 2023. A natural logarithmic transformation was applied to the original data, and analysis of covariance was conducted to adjust for age. The significance level (alpha) was set at 5% for all analyses. A violin plot was used to illustrate the distribution changes in semen parameters and serum hormones between 2022 and 2023, with each line representing the trend in the median for the corresponding weeks in both years.

Results

Information collection status

A total of 4,002 semen quality data points were collected from January 7, 2022, to April 30, 2022 (excluding azoospermia; n=426), while 5,085 semen quality data points were collected from January 7, 2023, to April 30, 2023 (excluding azoospermia; n=570). There was no statistical difference in the age of subjects between 2022 (mean age 32.57±5.47 years) and 2023 (mean age 32.65±5.39 years). However, the population from January 7 to February 6, 2023, with a mean age of 31.85±5.21 years, was younger than the population from January 7 to February 6, 2022, which had a mean age of 32.54±4.90 years. This difference may be attributed to the fact that younger individuals recover from COVID-19 faster. *Table 1* presents the monthly age distribution. Detailed data points for normal sperm morphology, FSH, LH, PRL, T, E2, SHBG, FTI, 25-OH-VD, OHP, and elastase were collected from January 7, 2022, to April 30, 2022, and from January 7, 2023, to April 30, 2023, and are listed in Table S1.

Effects of SARS-CoV-2 infection on semen quality

Figure S1 illustrates the changes in semen parameters between 2022, prior to the COVID-19 pandemic, and 2023, during the pandemic in China. The results indicated that semen volume, sperm concentration, and total sperm count in 2022 were significantly higher than those in 2023. *Table 2* presents the differences in semen parameters between the 2 years. A significant decrease in semen volume, sperm concentration, total sperm count, progressive sperm motility rate, and non-progressive sperm motility rate was noted following the nationwide relaxation of COVID-19 restrictions. Notably, the impact on semen volume and total sperm count persisted for an extended period until the observation cutoff; however, the effects on sperm concentration, progressive motility, and non-progressive motility were short-lived, lasting approximately one month. In addition, no significant pH changes were observed following SARS-CoV-2 infection.

The percentage of normal sperm morphology during the second month after the pandemic (February 7 to March 6, 2023) was lower than that during the same period in 2022 after adjusting for age. An increase in the incidence of sperm neck defects was also observed. After adjusting for age, the percentage of sperm head defects was lower in the first 2 months following the pandemic (from January 7 to March 6, 2023) than in the same period in 2022.

Conversely, the percentage of sperm tail defects in the second month after the pandemic (February 7 to March 6, 2023) was higher than that in the corresponding period in 2022. However, the percentages of sperm tail defects in the third (March 7 to April 6, 2023) and fourth months (April 7 to April 30, 2023) were lower than those observed in the same periods in 2022 (*Table 3*).

Effects of SARS-CoV-2 infection on hormone levels

Table 4 shows the differences in sex hormone levels before and after the nationwide relaxation of the COVID-19 restrictions. The COVID-19 pandemic appears to have induced a decrease in T, FTI, and elastase levels; however, this effect was relatively short-lived, lasting approximately one month. In contrast, the decreases in PRL and SHBG and the increase in E2 occurred later, around the second month following the onset of the pandemic (from February 7, 2023, to March 6, 2023), and these changes persisted until the conclusion of the observation period. Additionally, osteocalcin and 25-OH-VD levels were elevated compared with those recorded in 2022. No statistically significant changes were observed in the FSH, LH, or OHP levels after SARS-CoV-2 infection. Figure S2 shows the hormonal changes between 2022 (before the COVID-19 pandemic) and 2023 (during the pandemic), which revealed consistent trends.

Discussion

To investigate the impact of COVID-19 on semen quality, we compared semen quality parameters and serum hormone levels from January 7, 2023, to April 30, 2023 (pandemic experiencers) with data from January 7, 2022, to April 30, 2022 (non-pandemic experiencers) obtained from the Reproductive Centre of Henan Provincial People's Hospital. The population affected by the COVID-19 pandemic was selected shortly after the nationwide easing of COVID-19 restrictions, one month post-lifting. Data for the control population were collected during the same period in 2022 to control seasonal and temperature variations. The adverse effects of COVID-19 on sperm characteristics diminish by day 120 following diagnosis, in contrast to the effects observed at 14 days post-infection (14). However, the persistent deterioration of semen parameters observed after SARS-CoV-2 infection may be attributed to the permanent damage inflicted by the virus (15). Given that the duration of human spermatogenesis and epididymal sperm maturation is approximately 90 days, we divided the observation period into four months (01.07 to 02.06; 02.07 to 03.06; 03.07 to 04.06; 04.07 to 04.30) to assess both the short-term and relative long-term effects of the infection, as well as the temporal dynamics of recovery following viral infection. Our results indicate significant reductions in semen volume, sperm concentration, progressive motility, non-progressive motility, and total sperm count. Notably, these reductions primarily occurred during the first month of infection, with the exception of semen volume and total sperm count, which exhibited prolonged decreases that lasted until the observation cutoff time of approximately four months. Additionally, an increase in sperm neck defects was observed, suggesting that COVID-19 may have affected sperm necks. Infection also led to hormonal disruptions, as evidenced by reductions in PRL, T, SHBG, and FTI, along with increases in E2, osteocalcin, and 25-OH-VD. Furthermore, the effects of infection on T, FTI, and elastase were confined to approximately one month post-infection, whereas alterations in PRL, SHBG, and E2 manifested later.

In this study population, infections were predominantly caused by Omicron BA.5.2, and all subjects visited the reproductive center after recovering from the infection. Our findings indicated a reduction in semen quality, in contrast to the results of previous studies. Earlier research on mild COVID-19 reported no significant effects on semen parameters (9,10). This discrepancy may be attributed to the small sample sizes of these studies, which included only 37 and 189 volunteers, respectively. Additionally, a meta-analysis aligned with our findings demonstrated that mild or asymptomatic COVID-19 significantly diminished sperm concentration, total sperm count, progressive sperm motility, and normal sperm morphology (8). A pilot study involving men aged 19–45 years with COVID-19 also showed that while all semen samples tested negative for SARS-CoV-2, parameters such as semen volume, vitality, total motility, sperm concentration, total sperm count, percentage of normal form, percentage of cytoplasmic droplets, and fructose levels were significantly reduced in the first sample collected (16). Our study confirms that even mild infections can adversely affect semen quality.

Serum hormones play a crucial role in the regulation of spermatogenesis. One study reported that the levels of FSH, LH, PRL, and T were within the normal range in men recovering from COVID-19 (17). However, our results indicate a reduction in PRL, T, SHBG, and FTI levels, along with an increase in E2, osteocalcin, and 25-OH-VD levels.

Table 2 Semen quality before and after a nationwide loosening of coronavirus disease 2019 curbs

Parameter	2023	2022	P†	P‡
Semen volume (mL)				
Jan. 07 to Feb. 06	3.40 (2.40, 4.50)	3.80 (2.75, 4.90)	0.001**	<0.001**
Feb. 07 to Mar. 06	3.60 (2.50, 4.80)	3.90 (2.70, 5.00)	<0.001**	0.004**
Mar. 07 to Apr. 06	3.50 (2.40, 4.60)	3.60 (2.60, 4.80)	0.001**	0.002**
Apr. 07 to Apr. 30	3.40 (2.30, 4.70)	3.60 (2.60, 4.80)	0.01*	0.009**
Jan. 07 to Apr. 30	3.50 (2.40, 4.70)	3.70 (2.60, 4.90)	<0.001**	<0.001**
pH				
Jan. 07 to Feb. 06	7.40 (7.30, 7.40)	7.40 (7.30, 7.50)	0.20	0.12
Feb. 07 to Mar. 06	7.40 (7.30, 7.40)	7.40 (7.30, 7.40)	<0.001**	0.001**
Mar. 07 to Apr. 06	7.40 (7.30, 7.40)	7.40 (7.30, 7.40)	0.24	0.50
Apr. 07 to Apr. 30	7.40 (7.30, 7.40)	7.40 (7.30, 7.40)	0.26	0.23
Jan. 07 to Apr. 30	7.40 (7.30, 7.40)	7.40 (7.30, 7.40)	0.08	0.13
Sperm concentration (millions/mL)				
Jan. 07 to Feb. 06	31.70 (15.20, 56.70)	38.45 (21.60, 64.50)	<0.001**	<0.001**
Feb. 07 to Mar. 06	40.90 (21.60, 68.90)	42.70 (23.20, 72.60)	0.09	0.12
Mar. 07 to Apr. 06	46.15 (25.40, 75.90)	45.55 (24.70, 74.60)	0.76	0.96
Apr. 07 to Apr. 30	43.20 (24.10, 72.40)	45.70 (24.80, 73.50)	0.27	0.28
Jan. 07 to Apr. 30	41.40 (21.90, 70.10)	44.00 (23.80, 72.90)	<0.001**	<0.001**
Total sperm count (millions)				
Jan. 07 to Feb. 06	107.20 (45.15, 192.85)	147.36 (73.66, 253.57)	<0.001**	<0.001**
Feb. 07 to Mar. 06	141.03 (68.44, 254.80)	158.84 (76.56, 275.94)	0.002**	0.005**
Mar. 07 to Apr. 06	150.81 (77.00, 260.64)	160.45 (78.40, 287.42)	0.08	0.06
Apr. 07 to Apr. 30	138.02 (72.10, 248.16)	157.76 (81.28, 264.94)	0.01*	0.02*
Jan. 07 to Apr. 30	136.71 (67.36, 244.80)	157.59 (78.08, 276.33)	<0.001**	<0.001**
Progressive motility sperm rate (%)				
Jan. 07 to Feb. 06	26.90 (14.90, 41.60)	33.35 (19.80, 45.05)	<0.001**	<0.001**
Feb. 07 to Mar. 06	37.65 (23.30, 49.70)	35.30 (20.20, 48.40)	0.003**	<0.001**
Mar. 07 to Apr. 06	34.95 (19.80, 48.40)	34.60 (21.00, 47.90)	0.96	0.58
Apr. 07 to Apr. 30	34.15 (20.50, 49.00)	32.60 (20.00, 47.40)	0.07	0.08
Jan. 07 to Apr. 30	34.20 (19.80, 47.90)	34.25 (20.30, 47.80)	0.79	0.26
Non-progressive motility sperm rate (%)				
Jan. 07 to Feb. 06	8.10 (5.00, 12.10)	9.10 (6.30, 14.10)	<0.001**	<0.001**
Feb. 07 to Mar. 06	9.85 (6.50, 14.50)	10.10 (6.30, 15.00)	0.42	>0.99
Mar. 07 to Apr. 06	10.50 (6.80, 15.40)	10.10 (6.50, 15.70)	0.22	0.07
Apr. 07 to Apr. 30	9.40 (6.00, 13.80)	10.20 (6.10, 15.00)	0.04*	0.08
Jan. 07 to Apr. 30	9.60 (6.20, 14.20)	10.00 (6.30, 15.10)	0.005**	0.045*

Semen parameters are described as medians (Q1 and Q3) owing to the skewed distribution of the variables. *, P<0.05; **, P<0.01. †, Wilcoxon two-sample test; ‡, natural logarithmic conversion was performed on the original data and analysis of covariance adjusted for age.

Table 3 Sperm morphology before and after a nationwide loosening of coronavirus disease 2019 curbs

Parameter	2023	2022	P†	P‡
Normal morphology sperm rate (%)				
Jan. 07 to Feb. 06	4.3 (2.4, 5.8)	4.4 (2.4, 5.4)	0.70	0.76
Feb. 07 to Mar. 06	4.4 (2.4, 5.9)	4.9 (2.5, 5.9)	<0.001**	0.002**
Mar. 07 to Apr. 06	4.4 (2.4, 5.9)	4.4 (2.4, 5.9)	0.96	0.83
Apr. 07 to Apr. 30	4.4 (2.4, 5.9)	4.4 (2.4, 5.9)	0.64	0.89
Jan. 07 to Apr. 30	4.4 (2.4, 5.9)	4.4 (2.4, 5.9)	0.002**	0.005**
Head defect sperm rate (%)				
Jan. 07 to Feb. 06	80.0 (78.5, 82.4)	82.0 (80.9, 82.9)	<0.001**	<0.001**
Feb. 07 to Mar. 06	79.9 (78.3, 81.5)	81.0 (80.0, 82.4)	<0.001**	<0.001**
Mar. 07 to Apr. 06	80.4 (79.0, 82.1)	80.6 (79.1, 82.4)	0.10	0.56
Apr. 07 to Apr. 30	80.6 (79.0, 82.4)	81.0 (79.5, 82.4)	0.02	0.21
Jan. 07 to Apr. 30	80.0 (78.6, 82.0)	81.0 (79.6, 82.4)	<0.001**	<0.001**
Neck defect sperm rate (%)				
Jan. 07 to Feb. 06	12.7 (9.9, 12.7)	9.4 (8.4, 12.7)	<0.001**	<0.001**
Feb. 07 to Mar. 06	12.7 (10.2, 12.7)	10.3 (9.2, 12.7)	<0.001**	<0.001**
Mar. 07 to Apr. 06	11.9 (10.2, 12.7)	12.5 (9.4, 12.7)	0.002**	0.004**
Apr. 07 to Apr. 30	11.4 (10.2, 12.7)	10.8 (9.3, 12.7)	<0.001**	<0.001**
Jan. 07 to Apr. 30	12.4 (10.2, 12.7)	10.8 (9.2, 12.7)	<0.001**	<0.001**
Tail defect sperm rate (%)				
Jan. 07 to Feb. 06	3.9 (2.9, 4.4)	3.4 (2.9, 4.4)	0.10	0.12
Feb. 07 to Mar. 06	3.9 (2.9, 4.8)	3.4 (2.9, 4.4)	<0.001**	<0.001**
Mar. 07 to Apr. 06	3.9 (2.9, 4.4)	3.9 (2.9, 4.9)	0.02*	0.002**
Apr. 07 to Apr. 30	3.9 (2.9, 4.4)	4.3 (2.9, 4.9)	<0.001**	<0.001**
Jan. 07 to Apr. 30	3.9 (2.9, 4.4)	3.8 (2.9, 4.4)	0.048*	0.18

The sperm rate with normal morphology, head defect rate, neck defect rate, and tail defect rate are described as the median (Q1, Q3) owing to the skewed distribution of the variables. *, P<0.05; **, P<0.01. †, Wilcoxon two-sample test; ‡, natural logarithmic conversion was performed on the original data and analysis of covariance adjusted for age.

This finding is inconsistent with those of previous studies. A recent meta-analysis found no significant differences in sex-related hormone levels before and after infection in patients with mild or no symptoms (8). However, similar results have been observed in patients with severe symptoms, showing a reduction in T and an increase in LH and FSH levels (7,18). Furthermore, another meta-analysis demonstrated that COVID-19 decreases T levels and increases LH levels (5). Further studies are needed to elucidate the relationship between COVID-19 and sex-related hormones, which would be valuable in clarifying the mechanisms by which COVID-19 affects semen quality.

Numerous studies have documented a reduction in the effects of COVID-19 on sperm quality. However, our study design differs from those of previous studies. Our findings yield intriguing results that have not been previously reported. Four months post-infection, both semen volume and total sperm count were significantly lower than those recorded in the previous year. In contrast, sperm concentration, as well as progressive and non-progressive motility, exhibited a reduction only during the first month after infection. Additionally, the normal morphological

Table 4 Sex hormone levels before and after a nationwide loosening of coronavirus disease 2019 curbs

Parameter	2023	2022	P†	P‡
FSH (mIU/mL)				
Jan. 07 to Feb. 06	4.42 (3.17, 6.81)	4.47 (3.03, 7.08)	0.88	0.95
Feb. 07 to Mar. 06	4.61 (3.28, 6.64)	4.45 (3.23, 6.14)	0.09	0.10
Mar. 07 to Apr. 06	4.63 (3.33, 6.70)	4.62 (3.21, 6.66)	0.72	0.87
Apr. 07 to Apr. 30	4.53 (3.27, 6.67)	4.38 (3.25, 6.35)	0.31	0.44
Jan. 07 to Apr. 30	4.58 (3.28, 6.67)	4.50 (3.22, 6.45)	0.14	0.22
LH (mIU/mL)				
Jan. 07 to Feb. 06	4.09 (2.75, 5.62)	4.82 (2.93, 6.37)	0.03*	0.10
Feb. 07 to Mar. 06	4.51 (3.16, 6.44)	4.65 (3.29, 6.35)	0.55	0.66
Mar. 07 to Apr. 06	4.85 (3.49, 6.50)	4.64 (3.29, 6.72)	0.22	0.24
Apr. 07 to Apr. 30	4.79 (3.38, 6.53)	4.49 (3.27, 6.00)	0.09	0.15
Jan. 07 to Apr. 30	4.53 (3.15, 6.30)	4.63 (3.27, 6.43)	0.21	0.34
PRL (ng/mL)				
Jan. 07 to Feb. 06	10.76 (7.83, 15.13)	12.52 (9.36, 18.63)	0.004**	0.24
Feb. 07 to Mar. 06	10.81 (7.45, 14.73)	13.02 (9.95, 17.21)	<0.001**	<0.001**
Mar. 07 to Apr. 06	11.09 (8.22, 15.05)	12.34 (9.13, 15.51)	<0.001**	0.001**
Apr. 07 to Apr. 30	11.42 (8.39, 15.18)	13.68 (9.91, 17.92)	<0.001**	0.001**
Jan. 07 to Apr. 30	10.99 (7.86, 15.07)	12.85 (9.64, 16.85)	<0.001**	<0.001**
Testosterone (ng/mL)				
Jan. 07 to Feb. 06	3.02 (2.11, 4.05)	3.44 (2.66, 4.09)	<0.001**	0.02*
Feb. 07 to Mar. 06	3.30 (2.37, 4.48)	3.46 (2.44, 4.58)	0.13	0.10
Mar. 07 to Apr. 06	3.41 (2.52, 4.45)	3.45 (2.57, 4.76)	0.31	0.54
Apr. 07 to Apr. 30	3.53 (2.61, 4.70)	3.59 (2.60, 4.78)	0.98	0.78
Jan. 07 to Apr. 30	3.30 (2.38, 4.43)	3.46 (2.53, 4.61)	<0.001**	<0.001**
E2 (pg/mL)				
Jan. 07 to Feb. 06	23.03 (15.00, 32.16)	25.97 (18.42, 39.38)	<0.001**	0.006
Feb. 07 to Mar. 06	29.34 (22.88, 35.22)	28.43 (18.81, 38.30)	0.19	0.002**
Mar. 07 to Apr. 06	29.25 (23.99, 35.82)	25.29 (17.64, 33.67)	<0.001**	<0.001**
Apr. 07 to Apr. 30	30.22 (23.04, 36.76)	24.86 (16.56, 30.98)	<0.001**	0.001**
Jan. 07 to Apr. 30	28.46 (21.53, 35.00)	26.00 (17.97, 35.49)	<0.001**	<0.001**
SHBG (nmol/mL)				
Jan. 07 to Feb. 06	21.94 (17.08, 28.63)	20.70 (16.69, 27.83)	0.44	0.32
Feb. 07 to Mar. 06	22.57 (16.51, 30.98)	24.11 (18.35, 33.30)	<0.001**	<0.001**
Mar. 07 to Apr. 06	22.67 (17.01, 30.16)	24.31 (17.82, 33.87)	0.002**	0.004**
Apr. 07 to Apr. 30	23.41 (16.59, 30.46)	25.62 (19.44, 31.94)	0.003**	0.002**
Jan. 07 to Apr. 30	22.50 (16.76, 30.27)	24.26 (18.23, 33.19)	<0.001**	<0.001**
FTI (%)				
Jan. 07 to Feb. 06	49.81 (39.67, 60.84)	54.29 (44.10, 65.63)	0.003**	0.01*

Table 4 (*continued*)

Table 4 (*continued*)

Parameter	2023	2022	P†	P‡
Feb. 07 to Mar. 06	51.29 (40.12, 61.58)	49.26 (39.22, 60.55)	0.06	0.26
Mar. 07 to Apr. 06	50.43 (40.26, 62.68)	48.20 (38.48, 60.28)	0.02*	0.01*
Apr. 07 to Apr. 30	53.72 (42.68, 64.20)	48.18 (39.01, 59.74)	0.002**	0.007**
Jan. 07 to Apr. 30	51.11 (40.29, 62.33)	49.00 (38.99, 60.89)	0.003	0.06
25-OH-VD (ng/mL)				
Jan. 07 to Feb. 06	15.20 (11.76, 22.51)	10.17 (7.66, 13.99)	<0.001**	<0.001**
Feb. 07 to Mar. 06	15.63 (12.41, 20.87)	15.48 (12.00, 19.55)	0.06	0.01*
Mar. 07 to Apr. 06	16.69 (13.07, 21.71)	14.40 (11.21, 18.74)	<0.001**	<0.001**
Apr. 07 to Apr. 30	17.20 (13.24, 22.63)	14.29 (11.10, 18.93)	<0.001**	<0.001**
Jan. 07 to Apr. 30	16.11 (12.65, 21.75)	14.56 (11.29, 19.05)	<0.001**	<0.001**
Osteocalcin (ng/mL)				
Jan. 07 to Feb. 06	17.70 (14.56, 20.65)	16.09 (14.14, 18.45)	0.001**	0.009**
Feb. 07 to Mar. 06	17.33 (14.41, 21.12)	16.37 (13.36, 20.00)	0.002**	0.01*
Mar. 07 to Apr. 06	16.55 (13.85, 20.29)	16.78 (14.04, 20.82)	0.53	0.44
Apr. 07 to Apr. 30	17.45 (14.35, 21.01)	16.04 (13.00, 19.10)	<0.001**	<0.001**
Jan. 07 to Apr. 30	17.20 (14.27, 20.65)	16.38 (13.54, 20.00)	<0.001**	0.005**
OHP (ng/mL)				
Jan. 07 to Feb. 06	1.20 (0.86, 1.57)	1.20 (1.05, 1.46)	0.56	0.90
Feb. 07 to Mar. 06	1.12 (0.87, 1.46)	1.15 (0.90, 1.47)	0.09	0.06
Mar. 07 to Apr. 06	1.23 (095, 1.59)	1.12 (0.82, 1.45)	<0.001**	<0.001**
Apr. 07 to Apr. 30	1.12 (0.86, 1.47)	1.14 (0.88, 1.47)	0.89	0.45
Jan. 07 to Apr. 30	1.17 (0.88, 1.51)	1.14 (0.87, 1.46)	0.06	0.008**
Elastase (ng/mL)				
Jan. 07 to Feb. 06	326.30 (227.35, 466.40)	434.90 (313.30, 601.50)	<0.001**	<0.001**
Feb. 07 to Mar. 06	344.10 (235.70, 457.90)	359.60 (238.40, 496.30)	0.002	0.06
Mar. 07 to Apr. 06	342.50 (242.70, 459.20)	352.90 (204.00, 472.50)	0.54	0.04*
Apr. 07 to Apr. 30	338.10 (226.60, 481.10)	333.50 (209.70, 463.00)	0.56	0.33
Jan. 07 to Apr. 30	340.80 (233.80, 465.20)	359.20 (227.20, 484.40)	0.003**	0.35
Testosterone/luteinizing hormone				
Jan. 07 to Feb. 06	0.74 (0.47, 1.06)	0.72 (0.55, 1.14)	0.43	0.96
Feb. 07 to Mar. 06	0.75 (0.49, 1.10)	0.75 (0.51, 1.08)	0.73	0.62
Mar. 07 to Apr. 06	0.72 (0.51, 1.04)	0.76 (0.52, 1.09)	0.09	0.17
Apr. 07 to Apr. 30	0.75 (0.51, 1.14)	0.81 (0.55, 1.18)	0.15	0.36
Jan. 07 to Apr. 30	0.74 (0.50, 1.08)	0.76 (0.53, 1.09)	0.03*	0.04*

Serum hormone levels are expressed as medians (Q1, Q3). *, P<0.05; **, P<0.01. †, Wilcoxon two-sample test; ‡, natural logarithmic conversion was performed on the original data and analysis of covariance adjusted for age. 25-OH-VD, 25-hydroxy vitamin D; E2, estradiol; FSH, follicle-stimulating hormone; FTI, free testosterone index; LH, luteinizing hormone; OHP, osteocalcin and hydroxyprogesterone; PRL, prolactin; SHBG, sex hormone-binding globulin.

sperm rate in the second month after the pandemic declined, accompanied by an increase in the rate of sperm neck defects. Meta-analysis of male parameters before and after the COVID-19 pandemic revealed significant differences in concentrations, progressive movement, total movement, and normal morphology (19). However, conflicting results have indicated that there were no statistically significant differences in sperm motility and morphology between the COVID-19 negative and positive groups (20). Additionally, a report from India demonstrated that sperm parameter values, except for morphology, were higher in the pandemic group than in the pre-pandemic group, with the exception of morphology (21). The inconsistencies in these findings may stem from variations in the timing of semen sample collection following infection, suggesting that the effects of infection on semen may vary at different intervals post-infection. However, we observed that the sperm head defect percentage was lower in the first two months following the onset of the pandemic (from January 7, 2023, to March 6, 2023) than in the same period in 2022. This decrease in the head defect ratio may be attributable to an increase in the neck defect ratio, as the total defect ratio, when combined with the normal ratio in the head, neck, and tail positions, was 1.0. Additionally, we noted that sperm tail defects increased at 2 months post-pandemic, but subsequently decreased at 3 and 4 months. This pattern suggests that the situation may reverse as the infection subsides. A case report indicated that a moderate COVID-19 infection can rapidly induce azoospermia, which tends to resolve quickly as the infection diminishes (22). More comprehensive studies with larger sample sizes are necessary to gain a better understanding of changes in sperm characteristics before and after infection.

Mechanistically, in addition to attacking the lungs, the SARS-CoV-2 virus also has a great impact on the male genitourinary system (including the bladder, lower urinary tract, prostate, testicles and penis) (23). A cross-sectional study of men with mild to moderate SARS-CoV-2 infection found that approximately 40% had epididymitis, even in the absence of testicular symptoms (24). A prospective two-arm study found testicular tissue autopsy confirmed testicular inflammation and viral infiltration (7). Future research should incorporate longitudinal studies in men post-infection to elucidate the long-term effects of the virus. Semen quality is sensitive to temperature. Testicular heat damage leads to increased rates of apoptosis, and even a slight increase in temperature can disrupt spermatogenesis, eventually leading to fertility problems (25). One study showed that fever because of COVID-19 significantly reduced sperm concentration and progressive sperm motility (5). The most common symptoms of COVID-19 are nonspecific and include fever, cough, and myalgia (26), with most patients with COVID-19 experiencing a high fever lasting more than 3 days (27). Therefore, an increase in temperature within the male reproductive system may be the mechanism by which SARS-CoV-2 compromises the semen quality.

In addition to fever, other factors such as inflammation, oxidative stress, and hormonal changes also contribute to the biological processes through which SARS-CoV-2 affects sperm quality. SARS-CoV-2 infection is often associated with cytokine production, inflammation, cell death, and REDOX imbalances or oxidative stress, which induce the activation of NADPH oxidase, resulting in the production of superoxide, a reactive oxygen species (ROS) involved in the electron transport chain deterioration reaction (28). Insufficient levels of antioxidant enzymes and increased oxidative stress may lead to decreased semen quality. Hajizadeh and Tartibian (29) demonstrated that the COVID-19 group exhibited significantly higher levels of seminal plasma ACE2 enzymatic activity, interleukin-1β (IL-1β), IL-6, IL-8, IL-10, transforming growth factor-β (TGF-β), tumor necrosis factor-α (TNF-α), interferon-α (INF-α), IFN-γ, ROS, caspase-8, caspase-9, and caspase-3 activity, along with lower levels of SOD activity compared to the control group. This inflammatory phenomenon may also be triggered by the extracellular trap (ETosis) involved in the infected patient's sperm itself. The presence of infection is an important factor in inducing epididymal transit (ET) in semen (30). ETosis phenomenon refers to a type of cell death promoted by the depolymerization of nucleic acid DNA (31). A recent study found that in semen samples infected with SARS-CoV-2, the patient's sperm itself was involved in the ETosis process, also producing phenomena similar to those previously described in the systemic inflammatory response of COVID-19 (32). White blood cells can damage sperm DNA by increasing ROS levels, ultimately affecting male fertility (33). And after infection, white blood cells (such as PMN, monocytes, macrophages) are recruited into the male reproductive tract, which may cause ETosis to react to their own sperm, and MET may physically block sperm, inhibiting their movement after brief contact (34).

Changes in hormone levels may contribute to decreased semen quality. Spermatogenesis is regulated by T, SHBG, and FTI. Our study found a reduction in T, SHBG, and

FTI levels following recovery from infection. Inflammation resulting from infection may inhibit the gonadal axis, diminish the testicular response, and enhance T clearance during the acute phase of the disease (35). An experimental study that also indicated exposure to recombinant SARS-CoV-2 N protein may lower serum testosterone levels (36). Testosterone, a steroid sex hormone, is produced by Leydig cells. Testosterone drives male genital development and supports sperm production. A study have found that semen parameters such as sperm concentration, total motility, linear progressive motility and morphology are positively correlated with serum vitamin D and TT levels (37). SHBG is a glycoprotein that regulates the bioavailability of sex hormones. Low SHBG levels can lead to lower sperm count and sperm motility, which increases the risk of male infertility (38). Furthermore, it has been reported that a direct and positive relationship exists between serum vitamin D levels and overall semen quality, male reproductive potential, and testosterone levels (39) and that vitamin D3 supplementation enhances the T/LH ratio (40). However, our results did not show a similar trend. The observed increase in serum levels of osteocalcin and 25-OH-VD may have resulted from the nationwide relaxation of COVID-19 restrictions and outdoor activities in full sunlight. Increased sunlight exposure and physical activity can promote health and enhance semen quality. However, a decline in semen quality may indicate the presence of an infection because even mild infections can adversely affect semen quality. SARS-CoV-2 infection may lead to decreased semen quality by affecting sex hormone levels; however, the detailed mechanisms underlying these changes warrant further investigation.

Conclusions

Our findings revealed a reduction in semen quality and alterations in serum hormone levels after recovery from COVID-19 with mild symptoms. COVID-19 may reduce semen volume, sperm concentration, total sperm count, progressive motility, and non-progressive motility, and its influence on semen volume and total sperm count may persist for a long time. COVID-19 primarily affects the neck of spermatozoa. Furthermore, the alteration of serum hormones with a reduction in T, SHBG, and FTI and an increase in E2 may be among the reasons for the reduction in semen quality. However, the underlying mechanism requires further investigation.

Acknowledgments

None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tau.amegroups.com/article/view/10.21037/tau-24-562/rc

Data Sharing Statement: Available at https://tau.amegroups.com/article/view/10.21037/tau-24-562/dss

Peer Review File: Available at https://tau.amegroups.com/article/view/10.21037/tau-24-562/prf

Funding: This work was supported by the National Natural Science Foundation of China (No. 82273663) and the Youth project of National Natural Science Foundation of China (No. 82003489).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tau.amegroups.com/article/view/10.21037/tau-24-562/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Ethics Committee of Xinxiang Medical University (09/15/2017; No. XYLL—20170311) and Medical Ethics Committee of Henan Provincial People's Hospital [(2021) Lunga No. (41)]. Informed consent was taken from all the patients.

References

1. Auger J, Eustache F, Chevrier C, et al. Spatiotemporal trends in human semen quality. Nat Rev Urol 2022;19:597-626.
2. Virtanen HE, Jørgensen N, Toppari J. Semen quality in the 21(st) century. Nat Rev Urol 2017;14:120-30.
3. Wang H, He H, Wei Y, et al. Do phthalates and their metabolites cause poor semen quality? A systematic review and meta-analysis of epidemiological studies on risk of decline in sperm quality. Environ Sci Pollut Res Int 2023;30:34214-28.
4. Cardona Maya WD, Omolaoye TS, du Plessis SS. Re: The Impact of COVID-19 Vaccine on Sperm Quality. Eur Urol 2022;82:327-8.
5. Wang S, Zhang A, Pan Y, et al. Association between COVID-19 and Male Fertility: Systematic Review and Meta-Analysis of Observational Studies. World J Mens Health 2023;41:311-29.
6. Thomas T. Semen quality recovery following COVID-19. Nat Rev Urol 2023;20:131.
7. Enikeev D, Taratkin M, Morozov A, et al. Prospective two-arm study of the testicular function in patients with COVID-19. Andrology 2022;10:1047-56.
8. Che BW, Chen P, Yu Y, et al. Effects of mild/asymptomatic COVID-19 on semen parameters and sex-related hormone levels in men: a systematic review and meta-analysis. Asian J Androl 2023;25:382-8.
9. Edimiris P, Doehmen C, Müller L, et al. Mild COVID-19 has no detrimental effect on semen quality. Basic Clin Androl 2023;33:15.
10. Kabalkin Y, Bentov Y, Gil M, et al. Mild COVID-19 Was Not Associated with Impaired IVF Outcomes or Early Pregnancy Loss in IVF Patients. J Clin Med 2022;11:5265.
11. Ren J, Jin H, Zhang C, et al. Mixed exposure effect of seminal metals on semen quality, mediation of total antioxidant capacity, and moderation of GSTM1/GSTT1 gene deletion in Chinese reproductive-aged men. Environ Res 2023;229:115888.
12. Jia X, Dong T, Han Y, et al. Identifying the dose response relationship between seminal metal at low levels and semen quality using restricted cubic spline function. Chemosphere 2022;295:133805.
13. WHO laboratory manual for the examination and processing of human semen Sixth Edition. Available online: https://www.who.int/publications/i/item/9789240030787
14. Falahieh FM, Zarabadipour M, Mirani M, et al. Effects of moderate COVID-19 infection on semen oxidative status and parameters 14 and 120 days after diagnosis. Reprod Fertil Dev 2021;33:683-90.
15. Hamarat MB, Ozkent MS, Yilmaz B, et al. Effect of SARS-CoV-2 infection on semen parameters. Can Urol Assoc J 2022;16:E173-7.
16. Dipankar SP, Kumar T, Itagi ABH, et al. Semen Quality in Males Suffering From COVID-19: A Pilot Study. Cureus 2022;14:e31776.
17. Jiménez-López LA, Rojas-Ramírez DC, Martínez-Mier G, et al. Sperm concentrations do not correlate with semen parameters and hormone profiles in males recovered from COVID-19. Transl Androl Urol 2023;12:353-63.
18. Ma L, Xie W, Li D, et al. Evaluation of sex-related hormones and semen characteristics in reproductive-aged male COVID-19 patients. J Med Virol 2021;93:456-62.
19. Edele Santos D, Colonetti T, Rodrigues Uggioni ML, et al. Effects of COVID-19 or vaccines for SARS-COV-2 on sperm parameters: A systematic review and meta-analysis. J Reprod Immunol 2023;160:104140.
20. Aksak T, Satar DA, Bağci R, et al. Investigation of the effect of COVID-19 on sperm count, motility, and morphology. J Med Virol 2022;94:5201-5.
21. Kumar T, Jha K, Zabihullah M, et al. Effects of the COVID-19 pandemic on semen quality in male partners of infertile couples: a hospital-based observational study. Asian J Androl 2023;25:240-4.
22. Gharagozloo P, Cartagena S, Moazamian A, et al. Rapid impact of COVID-19 infection on semen quality: a case report. Transl Androl Urol 2022;11:110-5.
23. Connelly ZM, Whitaker D, Dullea A, et al. SARS-CoV-2 Effects on the Male Genitourinary System. Am J Clin Exp Urol 2022;10:199-209.
24. Carneiro F, Teixeira TA, Bernardes FS, et al. Radiological patterns of incidental epididymitis in mild-to-moderate COVID-19 patients revealed by colour Doppler ultrasound. Andrologia 2021;53:e13973.
25. Shahat AM, Rizzoto G, Kastelic JP. Amelioration of heat stress-induced damage to testes and sperm quality. Theriogenology 2020;158:84-96.
26. Umakanthan S, Sahu P, Ranade AV, et al. Origin, transmission, diagnosis and management of coronavirus disease 2019 (COVID-19). Postgrad Med J 2020;96:753-8.
27. Donders GGG, Bosmans E, Reumers J, et al. Sperm quality and absence of SARS-CoV-2 RNA in semen after COVID-19 infection: a prospective, observational study and validation of the SpermCOVID test. Fertil Steril 2022;117:287-96.
28. Fodor A, Tiperciuc B, Login C, et al. Endothelial

Dysfunction, Inflammation, and Oxidative Stress in COVID-19-Mechanisms and Therapeutic Targets. Oxid Med Cell Longev 2021;2021:8671713.
29. Hajizadeh Maleki B, Tartibian B. COVID-19 and male reproductive function: a prospective, longitudinal cohort study. Reproduction 2021;161:319-31.
30. Zambrano F, Schulz M, Pilatz A, et al. Increase of leucocyte-derived extracellular traps (ETs) in semen samples from human acute epididymitis patients-a pilot study. J Assist Reprod Genet 2020;37:2223-31.
31. Conceição-Silva F, Reis CSM, De Luca PM, et al. The Immune System Throws Its Traps: Cells and Their Extracellular Traps in Disease and Protection. Cells 2021;10:1891.
32. Hallak J, Caldini EG, Teixeira TA, et al. Transmission electron microscopy reveals the presence of SARS-CoV-2 in human spermatozoa associated with an ETosis-like response. Andrology 2024;12:1799-807.
33. Liu KS, Mao XD, Pan F, et al. Effect and mechanisms of reproductive tract infection on oxidative stress parameters, sperm DNA fragmentation, and semen quality in infertile males. Reprod Biol Endocrinol 2021;19:97.
34. Schulz M, Zambrano F, Schuppe HC, et al. Monocyte-derived extracellular trap (MET) formation induces aggregation and affects motility of human spermatozoa in vitro. Syst Biol Reprod Med 2019;65:357-66.
35. Lustig L, Guazzone VA, Theas MS, et al. Pathomechanisms of Autoimmune Based Testicular Inflammation. Front Immunol 2020;11:583135.
36. Lucio Carrasco CH, Noda P, Barbosa AP, et al. SARS-CoV-2 Nucleocapsid Protein is Associated With Lower Testosterone Levels: An Experimental Study. Front Physiol 2022;13:867444.
37. Kumari S, Singh K, Kumari S, et al. Association of Vitamin D and Reproductive Hormones With Semen Parameters in Infertile Men. Cureus 2021;13:e14511.
38. Wan Q, Xie Y, Zhou Y, et al. Research progress on the relationship between sex hormone-binding globulin and male reproductive system diseases. Andrologia 2021;53:e13893.
39. Ciccone IM, Costa EM, Pariz JR, et al. Serum vitamin D content is associated with semen parameters and serum testosterone levels in men. Asian J Androl 2021;23:52-8.
40. Maghsoumi-Norouzabad L, Zare Javid A, Mansoori A, et al. The effects of Vitamin D3 supplementation on Spermatogram and endocrine factors in asthenozoospermia infertile men: a randomized, triple blind, placebo-controlled clinical trial. Reprod Biol Endocrinol 2021;19:102.

Cite this article as: Zhang S, Zhang T, Ren J, Feng K, Xia Y, Lu H, Liu M, Guo H, Duan G, Zhang G, Cao J. A comparative study of the effects of the COVID-19 pandemic on semen quality based on a nationwide relaxation of COVID-19 restrictions in China at the end of 2022. Transl Androl Urol 2025;14(3):715-728. doi: 10.21037/tau-24-562