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COVID-19 vaccination and male fertility issues: Myth busted. Is taking COVID-19 vaccine the best choice for semen protection and male fertility from risky infection hazards?

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Abstract

The emerging coronavirus illness (COVID-19) pandemic is posing a global health hazard, with men being at a larger risk than women. There have been few publications on the andrological consequences of COVID-19 and its vaccines so far. To assuage vaccine fear stemming from concerns about fertility, the effect of inactivated whole-virus and viral vector vaccines on semen quality was investigated in 100 Egyptian men. The safety of COVID-19 vaccines on semen parameters was validated with no significant change in pre- and post-vaccination semen analyses in either type of vaccine. Following COVID-19 vaccination, we can declare male semen parameters as unaffected.

KEYWORDS
AstraZeneca COVID-19 vaccine, COVID-19, semen parameters, Sinopharm

1 | INTRODUCTION

From the Chinese city of Wuhan, just before the end of 2019, COVID-19, the disease caused by the SARS-CoV-2, was first discovered, found its way thereafter to the whole world declaring a new era changing the face of the universe as we once knew. Since then, more than 500 million cases and over 6 million deaths have been reported. It appears to be spreading at a faster rate, prompting the creation of a COVID-19 vaccine for public health purposes (Chan et al., 2020).

Through multiple pathogenic pathways, such as increased oxidative stress and increased DNA methylation and fragmentation, COVID-19 infection may affect sperm parameters and reduce male fertility. Angiotensin-converting enzyme 2 (ACE2) can cause direct harm to Leydig cells and spermatocytes. Another mechanism of testicular injury is the secondary immune and inflammatory response, which is heightened during a severe viral infection in the testicles due to an increased blood virus load in the blood. Furthermore, high temperatures that remain during active viral infection might disrupt the blood-testis barrier (BTB), allowing viruses to enter seminiferous tubules (Kumar & Kaur, 2021). COVID-19 can be associated with spermatogenesis dysregulation, regardless of whether the virus is present or not in the sperm (Bendayan & Boitrelle, 2021).

Planning an effective vaccination campaign will be critical to public health protection. Globally, mass vaccination against COVID-19 has begun using licensed vaccines. Fifty-eight vaccines against COVID-19 been produced and are in clinical testing (Best et al., 2021).

Two vaccines, Oxford– AstraZeneca chimpanzee adenovirus vectored vaccine (ChAdOx1 nCoV-19) (AZD1222) (AstraZeneca COVID-19 vaccine) and (WIV04 and HB02) (BBIBP-CorV) (Sinopharm) were available in Egypt at the time this study was initiated. The choice between these COVID-19 vaccines is based on availability, patient preference and the possibility of rare adverse events.

The AZD1222 vaccine—a vaccine based on an adenoviral vector-was developed by the University of Oxford in conjunction with AstraZeneca, a Swedish pharmaceutical company (Folegatti et al., 2020). The backbone of the vector is a replication-deficient chimpanzee adenovirus with a seroprevalence of 0%–9% in humans. The vector comprises full-length S protein genes as well as an adjuvant sequence (tissue plasminogen activator, tPA) (van Doremalen et al., 2020).

The BBIBP-CorV vaccines are whole-virus inactivated vaccines based on two separate SARS-CoV-2 isolates from Chinese patients; each have an aluminium hydroxide adjuvant. HB02 is also known as BBIBP-CorV. elicited neutralizing and binding antibody responses in healthy individuals; no severe reactions were reported (Xia et al., 2020; Xia et al., 2021). It's nearly identical: viruses grown in Vero cells,

inactivated with -propiolactone, and absorbed in aluminium. The virus strain employed was HB02, which was isolated from a BAL sample of a Wuhan hospitalized patient (Wang et al., 2020).

COVID-19 vaccine research is advancing at breakneck pace. Any COVID-19 vaccine's success will hinge on the public's trust and confidence in it. Pre- and post-vaccine data, as well as semen parameters, are absent. So, to address vaccination safety issues related to fertility, the parameters of the sperm before and after the second dosage of COVID-19 vaccination are compared in the current work.

2 | SUBJECTS AND METHODS

2.1 | Study design and participants

A prospective cohort study was designed and carried out at Dermatology, Venereology and Andrology Department in Benha University during the period from March 2021 to December 2021.

It included 100 apparently healthy male participants aged 20–45 years scheduled for COVID-19 vaccination through Egyptian Ministry of Health immunization program. The Oxford/AstraZeneca COVID-19 vaccine was administered as two 0.5 ml intramuscular injections, 12 weeks apart. While the Sinopharm vaccine was given in two doses of 0.5 ml intramuscular injections, separated by 21 days.

2.2 | Ethics statement

The local Research Ethics Committee gave its approval to the project. Subjects were contacted about their participation in the study once they were identified, at which time the study's specifics were presented and they were advised about their voluntary engagement in the study. Informed written consents were collected from individuals who were willing to participate. The technique was outlined in accordance with the Helsinki Declaration.

2.3 | Specimen collection and processing

Pre-screening was done on the men to make sure they did not have any fertility difficulties. To rule out possible reasons of male infertility, such as varicocele, a complete medical history and clinical examination were performed. All subjects who were unable to consent, were severely ill, had ejaculatory dysfunctions, had a history of sexually transmissible infections, had a history of male factor infertility, or COVID-19 symptoms or a positive test within the last 90 days were omitted from the study. Individuals with oligo-zoospermia (sperm concentration < 15 million/mL) were not excluded.

Participants' age-matched samples were obtained before and after vaccine doses over the same period. Participants gave a semen sample following an abstinence period of 2–7 days, before receiving the first vaccine dosage, and 70 days after receiving the second.

The WHO guidelines for the testing of human semen were followed to determine semen quality parameters, which were standardized by the WHO and distributed through the publication of the WHO Laboratory Manual for the Examination and Processing of Human Semen (5th ed.) (WHO, 2010).

2.4 | Statistical analysis

SPSS version 28 was used for data administration and statistical analysis (IBM, Armonk, New York, USA). The Kolmogorov–Smirnov test

TABLE 1 Semen characteristics pre and post Sinopharm vaccination

			Sinopharm vaccine		
			Pre	Post	*p*-value
Volume (ml)	Mean ± SD		3.4 ± 1.3	3.3 ± 1.2	0.077
PH	Mean ± SD		7.6 ± 0.1	7.6 ± 0.1	–
Colour	Grey opalescent	*n* (%)	50 (100.0)	50 (100.0)	–
Odour	Normal	*n* (%)	50 (100.0)	50 (100.0)	–
Viscosity	Low	*n* (%)	40 (80.0)	39 (78.0)	1.0
	Moderate	*n* (%)	10 (20)	11 (22.0)	
Concentration (mil/ml)	Median (range)		57.9 (15–170.5)	54.65 (15–170.6)	0.060
Liquefaction time (min)	Mean ± SD		26 ± 8	26 ± 7	0.062
Progressive motility (%)	Mean ± SD		35.9 ± 7.9	35.8 ± 8.4	0.760
Total motility con (mil/ml)	Median (range)		36.6 (5.5–100.9)	36.2 (5.5–100.9)	0.948
Total number (million)	Median (range)		107.6 (16.4–335.2)	110.1 (16.4–335.2)	0.390
Percent motility	Mean ± SD		59.5 ± 11.4	58.2 ± 10.1	0.080
Morphology index	Mean ± SD		50.6 ± 12.1	50.1 ± 11.7	0.066

Note: Paired *t*-test or Wilcoxon signed ranks test was used for quantitative variables. McNemar's test was used for viscosity.

and direct data visualization approaches were used to check for normalcy in quantitative data. Numerical data were reported as means and standard deviations or medians and ranges based on normality tests. Numbers and percentages were used to summarize categorical data. Within groups, comparisons were done using paired t-test or Wilcoxon's signed ranks test for normally and non-normally distributed quantitative data, respectively. Categorical data were compared within groups using McNemar's test. For normally and non-normally distributed quantitative data, comparisons between groups were made using the independent *t*-test or the Mann–Whitney *U* test, respectively. The Chi-square test was used to compare categorical data between groups. All statistical tests were conducted on a two-sided basis. Significant P values were defined as those less than 0.05.

3 | RESULTS

This study encompassed 100 individuals; 50 individuals with a mean age of 34 ± 7 years received two doses of the Sinopharm vaccine, and 50 individuals with a mean age of 34 ± 6 years received two doses of the AstraZeneca vaccine. All semen characteristics were compared pre- and post-vaccination for both types.

3.1 | Sinopharm vaccination

No significant differences were noted in all semen characteristics post Sinopharm vaccination, including volume ($p = 0.077$), PH, colour, odour, viscosity ($p = 1.0$), concentration ($p = 0.060$),

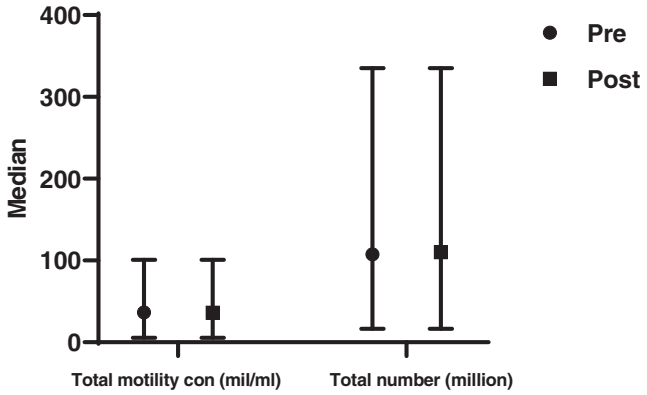

FIGURE 1 Total motility concentration and total number pre and post Sinopharm vaccination

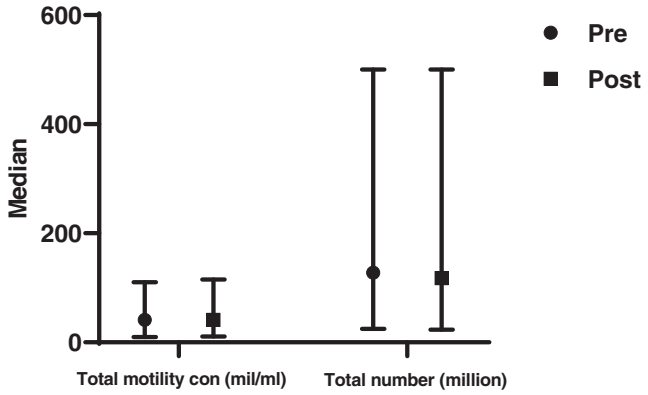

FIGURE 2 Total motility concentration and total number pre and post AstraZaeneca vaccination

TABLE 2 Semen characteristics pre and post AstraZeneca vaccination

			AstraZeneca vaccine		
			Pre	Post	*p*-value
Volume (ml)	Mean ± SD		3.7 ± 1.8	3.7 ± 1.8	–
PH	Mean ± SD		7.6 ± 0.1	7.6 ± 0.1	–
Colour	Grey opalescent	*n* (%)	50 (100.0)	50 (100.0)	-
Odour	Normal	*n* (%)	50 (100.0)	50 (100.0)	
Viscosity	Low	*n* (%)	41 (82.0)	41 (82.0)	–
	Moderate	*n* (%)	7 (14.0)	7 (14.0)	
	High	*n* (%)	2 (4.0)	2 (4.0)	
Concentration (mil/ml)	Median (range)		67.8 (19.8–133.3)	68.2 (20.4–133.3)	0.707
Liquefaction time (min)	Mean ± SD		28 ± 9	28 ± 9	–
Progressive motility (%)	Mean ± SD		37.7 ± 10.3	37.4 ± 10.2	0.402
Total motility Con (mil/ml)	Median (range)		41.3 (9.9–110.3)	41.1 (10.5–115.3)	0.168
Total number (million)	Median (range)		127.7 (24.5–500.4)	117.9 (23.2–500.4)	0.301
Percent motility	Mean ± SD		56 ± 11	54.9 ± 10.7	0.078
Morphology index	Mean ± SD		51.8 ± 8.3	51.1 ± 8	0.087

Note: Paired *t*-test or Wilcoxon signed ranks test was used.

liquefaction time ($p = 0.062$), progressive motility ($p = 0.760$), total motility concentration ($p = 0.948$), total number ($p = 0.390$), percent motility ($p = 0.080$), and morphology index ($p = 0.066$) (Table 1 and Figure 1).

3.2 | AstraZeneca vaccination

No significant differences were noted in all semen characteristics post-AstraZeneca vaccination, including volume, PH, colour, odour,

TABLE 3 Semen physical characteristics pre- and post-vaccination in the studied groups

			AstraZeneca ($n = 50$)	Sinopharm ($n = 50$)	p-value
Volume					
Pre	Mean ± SD		3.7 ± 1.8	3.4 ± 1.3	0.309
Post	Mean ± SD		3.7 ± 1.8	3.3 ± 1.2	0.177
pH					
Pre	Mean ± SD		7.6 ± 0.1	7.6 ± 0.1	0.545
Post	Mean ± SD		7.6 ± 0.1	7.6 ± 0.1	0.545
Colour					
Pre	Grey opalescent	*n* (%)	50 (100.0)	50 (100.0)	–
Post	Grey opalescent	*n* (%)	50 (100.0)	50 (100.0)	–
Odour					
Pre	Normal	*n* (%)	50 (100.0)	50 (100.0)	–
Post	Normal	*n* (%)	50 (100.0)	50 (100.0)	–
Viscosity					
Pre	Low	*n* (%)	41 (82.0)	40 (80.0)	0.281
	Moderate	*n* (%)	7 (14.0)	10 (20)	
	High	*n* (%)	2 (4.0)	0 (0.0)	
Post	Low	*n* (%)	41 (82.0)	39 (78.0)	0.230
	Moderate	*n* (%)	7 (14.0)	11 (22.0)	
	High	*n* (%)	2 (4.0)	0 (0.0)	
Concentration					
Pre	Median (range)		67.8 (19.8–133.3)	57.9 (15–170.5)	0.093
Post	Median (range)		68.2 (20.4–133.3)	54.65 (15–170.6)	0.098
Liquefaction time (min)					
Pre	Mean ± SD		28 ± 9	26 ± 8	0.312
Post	Mean ± SD		28 ± 9	26 ± 7	0.186
Progressive motility (%)					
Pre	Mean ± SD		37.7 ± 10.3	35.9 ± 7.9	0.328
Post	Mean ± SD		37.4 ± 10.2	35.8 ± 8.4	0.373
Total motility Con (mil/ml)					
Pre	Median (range)		41.3 (9.9–110.3)	36.6 (5.5–100.9)	0.145
Post	Median (range)		41.1 (10.5–115.3)	36.2 (5.5–100.9)	0.162
Total number (million)					
Pre	Median (range)		127.7 (24.5–500.4)	107.6 (16.4–335.2)	0.497
Post	Median (range)		117.9 (23.2–500.4)	110.1 (16.4–335.2)	0.478
Percent motility					
Pre	Mean ± SD		56 ± 11	59.5 ± 11.4	0.127
Post	Mean ± SD		54.9 ± 10.7	58.2 ± 10.1	0.121
Morphology index					
Pre	Mean ± SD		51.8 ± 8.3	50.6 ± 12.1	0.575
Post	Mean ± SD		51.1 ± 8	50.1 ± 11.7	0.617

Note: Independent *t*-test or Mann Whitney *U* test was used. Viscosity was compared using the Chi-square test.

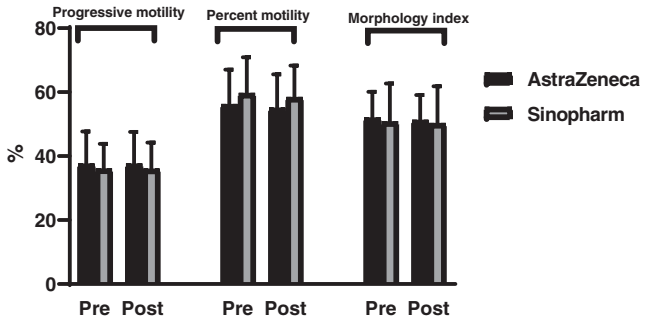

FIGURE 3 Progressive motility, percent motility, and morphology index pre- and post-vaccination in both groups

viscosity, concentration ($p = 0.707$), liquefaction time, progressive motility ($p = 0.402$), total motility concentration ($p = 0.168$), total number ($p = 0.301$), percent motility ($p = 0.078$), and morphology index ($p = 0.087$) (Table 2 and Figure 2).

3.3 | AstraZeneca versus Sinopharm

No significant differences were observed between both groups pre and post vaccination regarding volume ($p = 0.306$ and 0.177, respectively), pH ($p = 0.545$), colour, odour, viscosity ($p = 0.281$ and 0.230, respectively), concentration ($p = 0.093$ and 0.098, respectively), liquefaction time ($p = 0.312$ and 0.186, respectively), progressive motility ($p = 0.328$ and 0.373, respectively), total motility concentration ($p = 0.145$ and 0.162, respectively), total number ($p = 0.497$ and 0.478), percent motility ($p = 0.127$ and 0.121, respectively), and morphology index ($p = 0.575$ and 0.617, respectively) (Table 3 and Figure 3).

4 | DISCUSSION

The SARS-CoV-2 is the revolutionary pandemic that has altered our understanding of the world. Vaccination is currently at the center of the WHO's recommended preventive strategies. According to Liu and Tao (2021), patients with moderate COVID-19 infection showed considerably lower sperm quantity and quality than patients with mild infection or healthy subjects. The available research suggests that COVID-19 infection could be dangerous to a man's reproductive system. Vaccines and their effects on sperm parameters, on the other hand, are poorly understood.

It was observed that Google searches for the COVID-19 vaccine and fertility considerably rose after the vaccine Emergency Use Authorization (Diaz et al., 2021). To alleviate vaccine apprehension based on fertility concerns, in this study semen analysis before and after 2 doses of 2 types of COVID-19 vaccines was evaluated to find out their impact on semen parameters in men.

To our best knowledge, we are the first to investigate the link between semen parameter changes and reproductive function in apparently healthy fertile male subjects receiving inactivated whole-virus or viral vector COVID-19 vaccines.

Scant data were found regarding effect of COVID-19 vaccine on sperm variables. A study by Gonzalez and colleagues was performed to address effect of COVID -19 mRNA vaccines on semen parameters. Among a small cohort of healthy men and after two doses of COVID-19 mRNA vaccination, they detected no significant reductions in any sperm parameter (Gonzalez et al., 2021). They explained their results by the hypothesis that the vaccine that does not contain a viral vector is unlikely to affect semen parameters.

Similarly, Orvieto et al. (2021) focused on the impact of the mRNA SARS-CoV-2 vaccine on 36 ART-treated couples and found no significant changes in male and female fertility indices when pre- and post- vaccination data were analysed.

These findings were reinforced by ours. Semen quality is not affected by COVID-19 vaccination in apparently healthy fertile men. This study validated these findings for both inactivated whole-virus and viral vector vaccines. Of notice, even men with oligozoospermia did not show further drop in their sperm count.

In the same context, Reschini et al. (2022) declared that both COVID-10 vaccines; messenger RNA (mRNA) vaccines, and viral vector vaccines had no effect on sperm quality in males using ART and should be regarded safe for men's reproductive health.

Furthermore, Safrai et al. (2021), declared that BNT162b2 mRNA Covid-19 vaccine does not impair sperm parameters. Thus, recommending these vaccines to couples planning to have children, with the caveat that vaccination does not damage sperm, although SARS-CoV-2 infection does. Only about 16 percent of men experienced fever after receiving the second dosage of the Pfizer/BioNtech vaccine, according to Kumar and Kaur (2021), which could have resulted in temporary sperm production decreases equivalent to or less than if the man developed fever from COVID-19 or for other reasons.

Moreover, the magnitude of change, according to Keel (2006), is within the range of typical individual variation and may be impacted by the mean reversion. They hypothesized that the rise was related to the longer period of abstinence before the second specimen in their own work.

In general, when counselling male patients who are concerned about unfounded male fertility effects of the COVID-19 vaccine, we can now clarify an important point to keep in mind: COVID-19 infection can injure the testes and alter the properties of sperm while, the vaccine may help prevent illness and so maintain reproductive potential. Furthermore, semen parameters appear to be unaffected in the short term.

The small number of men who participated, the study's restricted generalization of results beyond youthful healthy males, the lack of a control group and the short follow-up are all flaws. Furthermore, sperm analysis is an imprecise predictor of reproductive capacity, despite being the cornerstone of male fertility assessment. Regardless, the study's time range encompasses the complete sperm life span.

5 | CONCLUSIONS

Until further research with long-term data is published, its concluded that COVID-19 vaccines are safe on male semen parameters. This is

valid for both adenoviral vector vaccine (namely AstraZeneca) and inactivated whole-virion vaccine (namely Sinopharm).

CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data available with author when requested

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