A Reversible Drawback Effects Of COVID 19 mRNA Vaccine On Semen Parameters Of Fertile Male

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Abstract

Objectives: To determine the impact of COVID-19 vaccine on semen parameters in an Egyptian population sample of previously proved fertile males.

Design: Prospective observational research.

Patients and methods: The study was conducted on 30 males proved to have normal semen parameters, on list of ICSI due to female factors of infertility, and received the two doses of mRNA COVID vaccine. Following the second dose of the vaccine, two samples of semen were obtained from all the subjects under the study, after 3 months and 6 months respectively . Parameters of sperm quality were examined. All semen specimens were tested throughout conformance with WHO sperm assessment guidance.

Results: The participants average age was (38.13 ± 5.27); at different period of follow up (at baseline, after 3 months and after 6 months). There was no significant difference in sperm volume among variables after 3 and 6 months (p3= 0.118). There was a significant difference in the sperm concentration between the base line and after 3 months (p1= 0.003); there was no significant difference in sperm concentration between base line and after 6 months (p2= 0.211). There was a significant difference in sperm count among variables after 3 and 6 months (p3= 0.005).

There was a significant difference in sperm progressive motility (%) between base line and after 3 months (p1= 0.007). There was no significant difference in sperm morphology (percentage) between variables after 3 and 6 months (p3= 0.096). There was significant difference in sperm DNA fragmentation (%) between base line and after 3 months (p1= 0.011). There was no significant difference in non –sperm cells /ml among variables after 3 and 6 months (p3= 0.186).

Conclusion: The sperm count and concentration, sperm motility were decreased 3 months post vaccination and return to average 6 months post vaccination. The sperm DNA fragmentation index is raised beyond limits 3 months post vaccination and return to normal limits 6 months post vaccination. The effect of mRNA vaccine on semen parameters is transient and reversible . The criteria of the sperm after obtaining the vaccine of COVID-19 were mostly within normal range intervals. The findings support the notion that COVID-19 vaccine is free from risk.

Keywords: COVID-19 vaccine, Sperm DNA fragmentation, Sperm parameters.

Background

The World Health Organization has announced coronavirus disease 2019 (COVID-19) as a global pandemic since March 11, 2020 .[1] The pandemic, also known as the SARS-CoV-2 pandemic, has imposed huge pressure on health care systems around the world .[2,3]

The SARS-CoV2 mainly transmits through respiratory droplets [4] and has been also observed in different biological fluids including blood, urine, and feaces .[5] Due to the blood-testis barrier (BTB), testis is partially immune to many microorganisms [6]; however, some viruses such as the mumps virus have the ability to cross the BTB and cause localized testis inflammation in forms of orchitis [8]. On the other hand, angiotensin-converting enzyme 2 (ACE2) and viral spike (S) protein, the mediators for SARS–COV-2 entrance into the target cells, mainly exist in human testis . [9,10]

Several findings indicated sexual transfer of COVID-19 infection via males; in addition to the existence of the virus in testis and semen in the acute and recovering phases.[11] SARS-CoV2 has the capacity to penetrate the male genital tract due to an incomplete blood-testis/vas deferens/epididymal barrier, particularly when there is systemic local inflammatory condition.[12] Furthermore, due to the virus's inability to reproduce inside the sex organs, it may hang most likely due to the testicle special immunity. Nonetheless, the viruses existence in sperms is not uncommon.[13,14,15] Oxidative stress and increased apoptosis are between the factors proposed to explain the negative effects of COVID-19 on the quality of sperms[16,17] , in addition to synergistic negative effects of impaired (ACE 2) signaling pathway .[18,19]

Generally speaking, the COVID19 vaccine has been demonstrated to be greatly efficacious and useful for the general public.[20,21] Two widely used types of COVID -19 vaccines, Messenger RNA (mRNA) vaccine and inactivated virus vaccine. Messenger RNA vaccine is taken in two doses 28 days apart whereas the inactivated virus vaccine is given in two doses 14 days apart.[21]

The present study concerns with detection of the influence of mRNA vaccine ,after two doses ,on the different semen parameters in previously proven fertile males on waiting list of ICSI due to female factors.

Materials and method

Study setting : This prospective observational research was done at a single large reputable institution in Alexandria.

Study Design : Prospective observational research.

Study subjects : The study was conducted on 30 males proved to have normal semen parameters, on list of ICSI due to female factors of infertility ,and received the two doses of mRNA COVID vaccine.

Sample size calculation: The information was gathered and entered into the computer. The Statistical Package for Social Sciences (SPSS/version 22) software was used for statistical analysis. The F-test (ANOVA) was used, followed by a hoc test to detect the significance between the two groups. The significance level was set at 0.05.

Sampling technique : Following the second dose of the vaccine, two samples of semen were obtained from all the subjects under the study , after 3 months and 6 months respectively . Parameters of sperm quality were examined. All semen specimens were tested throughout conformance with WHO sperm assessment guidance.

All semen samples were measured for sperm volume in ml , sperm concentration / ml , Total sperm count in the specimen , sperm progressive motility , sperm morphology , sperm DNA fragmentation index , and non- sperm cells / ml . The WHO laboratory manual for the examination and processing of human semen , variables and Cut- off values used in the study are shown in the next table **(Table 1)**.

variable	Cut- off value
Sperm volume	< 1.5 ml
Sperm concentration	< 15 million / ml
Total Sperm count	< 39 million
Sperm progressive motility (A+B)	< 32%
Sperm morphology	< 4%
Non- Sperm cells	> 1 million / ml

Sperm DNA fragmentation index (DFI) was determined; using the following interpretation values ≤ 15% (good fertility potential) , 15-25% (average fertility potential) ,and > 25% (poor fertility potential) **(Evenson et al., 2002)** .

The values of semen parameters in the basal specimens before the vaccine and the values of semen parameters after two doses of mRNA vaccine, taken three and six months respectively, are compared to detect any significant changes caused by the effect of the vaccine.

Results

Our study population included 30 males aged between (29-46) years with a mean age of (38.13 ± 5.27) , (56.67%) were aged between (30-40) years, (36.67%) were >40 years , and (6.67%) were < 30 years. **The age of the studied subjects is depicted in Table 2 .**

Table (2): Age distribution among the studied group

Age	No	%
<30 30-40 >40	2 17 11	6.67 56.67 36.67
Range Mean SD	29-46 38.13 5.27	

At different period of follow up, sperm volume, concentration and total sperm count were described in Table (3).

The mean sperm volume at baseline was (2.88 ± 0.62); after 3 months (2.67 ± 0.57) and after 6 months (2.85 ± 0.61). There was no significant difference in sperm volume between base line and after 3 months (p1= 0.092); There was no significant difference in sperm volume among base line and after 6 months (p2= 0.439) and there was no significant difference in sperm volume among variables after 3 and 6 months (p3= 0.118).

The mean sperm concentration at baseline was (29.08 ± 5.30); after 3 months (18.6 ±3.58) and after 6 months (28.92 ± 5.12).

There was a significant difference in the sperm concentration between the base line and after 3 months (p1= 0.003); there was no significant difference in sperm concentration between base line and after 6 months (p2= 0.211) and there was a significant difference in sperm concentration between variables after 3 and 6 months (p3= 0.001). The mean sperm concentration declined

3 months post-vaccination and return to average values 6 months post-vaccination .

The mean sperm count at baseline was (71.32 ± 21.84); after 3 months (28.1 ± 8.21) and after 6 months (68.00 ± 21.64).

There was a significant difference in sperm count between base line and after 3 months (p1= 0.001) there was no significant difference in sperm count between base line and after 6 months (p2= 0.263) and there was a significant difference in sperm count among variables after 3 and 6 months (p3= 0.005). The mean sperm count declined 3 months post-vaccination and return to average values 6 months post-vaccination.

Table (3): Sperm volume, concentration and total sperm count at different period of follow up

	At base line "n=30"	After 3 months "n=30"	After 6 months "n=30"	ANOVA P value	P1 P2 P3
Sperm volume (ml)					
Range	1.8-3.9	1.6-3.7	1.8-3.9		0.092
Mean	2.88	2.67	2.85	2.01	0.439
SD	0.62	0.57	0.61	0.465 N.S.	0.118
Sperm concentration (million/ml)					
Range	20.1-37.5	12-25	19.8-36.3		0.003*
Mean	29.08	18.6	28.92	29.85	0.211
SD	5.30	3.58	5.12	0.002*	0.001*
Total sperm count (million)					
Range	41.8-103.3	24-46	41.6-107.0		0.001*
Mean	71.32	28.1	68.00	24.1	0.236
SD	21.84	8.21	21.64	0.003*	0.005*

P1 comparison between base line and after 3 months.
P2 comparison between base line and after 6 months.
P3 comparison between variables after 3 and 6 months.

Sperm progressive motility and sperm morphology at different period of follow up were described in Table (4).

The mean sperm progressive motility (%) at baseline was (46.50 ± 5.04); after 3 months (30.0± 5.21) and after 6 months (42.5 ± 5.11). There was a significant difference in sperm progressive motility (%) between base line and after 3 months (p1= 0.007); and There was a significant difference in sperm progressive movement (percentage) between variables after 3 and 6 months (p3= 0.003).

The mean sperm morphological characters (%) at baseline was (8.97 ± 1.83); after 3 months (8.29 ± 1.69) and after 6 months (8.88 ± 1.80). There was no significant difference in sperm morphological characters (percentage) among base line and after 3 months (p1= 0.071); there was no significant difference in sperm morphology (percentage) between base line and after 6 months (p2= 0.430) and there was no significant difference in sperm morphology (percentage) between variables after 3 and 6 months (p3= 0.096).

Table (4): Sperm progressive motility and sperm morphology at different period of follow up.

	At base line "n=30"	After 3 months "n=30"	After 6 months "n=30"	ANOVA P value	P1 P2 P3
Sperm progressive motility (%)					
Range	39-56	18-42	37.3-55.0		0.007*
Mean	46.50	30.0	42.5	20.1	0.278
SD	5.04	5.21	5.11	0.003*	0.003*
Sperm morphology (%)					
Range	6-12	5.5-11.0	5.8-11.6		0.071
Mean	8.97	8.29	8.88	5.21	0.430
SD	1.83	1.69	1.80	0.106	0.096

Sperm DNA fragmentation index and non –sperm cells /ml results are showed in Table(5).

The mean sperm DNA fragmentation (%) at baseline was (22.3 ± 4.5); after 3 months (31.5 ± 5.12) and after 6 months (18.2 ± 3.01). There was significant difference in sperm DNA fragmentation (%) between base line and after 3 months (p1= 0.011) and there was a significant difference in sperm DNA fragmentation (%) between base line and among variables after 3 and 6 months (p3=0.017).

There was no significant difference in non –sperm cells /ml between base line and after 3 months (p1= 0.162); there was no significant difference in non –sperm cells /ml among base line and after 6 months (p2= 0.475) and there was no significant difference in non –sperm cells /ml among variables after 3 and 6 months (p3= 0.186).

Table (5): Sperm DNA fragmentation, non –sperm cell at different period of follow up.

	At base line "n=30"	After 3 months "n=22"	After 6 months "n=19"	ANOVA P value	P1 P2 P3
Sperm DNA fragmentation (%)					
Range	16-24	20-42	17-26		0.011*
Mean	22.3	31.5	18.2	16.41	0.097
SD	4.5	5.12	3.01	0.003*	0.017*
Non-sperm cells million/ml					
Range	0.4-0.9	0.4-1.0	0.4-0.9		0.162
Mean	0.62	0.67	0.62	3.12	0.475
SD	0.17	0.19	0.18	0.167	0.186

Discussion

COVID-19 infection has been found to affect negatively the reproduction in men, whether due to local or systemic inflammatory conditions (Orvieto et al., 2021).[20] The possibilities of sexual transfer of COVID-19 and influence on the reproductive axis were discussed in many previous researches. COVID-19 infection, according to Ma et al. (2020),[17] could result in altered sex hormone production and reduced fertility. Holtmann et al. (2020)[10] postulated that disease could affect sperm production and found that medium disease lowered semen grade in a significant manner when compared to controls.

The testicles don't produce enough of the male sex hormone testosterone in men recovered from COVID-19 (Salonia et al., 2022).[24] There is small proof that various COVID-19 vaccinations affect sperm parameters or male fertility. Evidence of (mRNA) vaccines, viral vectors vaccines' short- to medium-term protection is accumulating (Reschini et al., 2022).[22]

The present study involved (30) cases with mean age (38.13 ± 5.27); in addition, more than half of cases were aged between (30-40) years.

Similar findings were obtained in previous studies; the study by Lifshitz et al., (2022)[15] included seventy five reproductive males with an average age of (38.6 4.3).Reschini et al., (2022)[22] study included 106 people with a median age of 39 [36–42] years. The average age of participants in the Safrai et al., (2021)[23] study was 37.1 years (±6.6), and the average time from first vaccine dose to sample collection was 33.6 days (± 20.2).

In the current study, there was no significant difference in sperm quantity among variables after 3 and 6 months (p3= 0.118). The mean sperm concentration declined 3 months post-vaccination and return to average values 6 months post-vaccination . The mean sperm count declined 3 months post-vaccination and return to average values 6 months post-vaccination.

Orvieto et al., (2021)[20] investigated thirty six married people who had IVF with sequential ovulatory stimuli periods before and after obtaining the messenger RNA COVID-19 vaccine. The Infertility factors, quantity of ovarian follicles, conception fee, and semen evaluations revealed no differences. Furthermore, after vaccination, the male partner's sperm parameters remained unchanged.

According to the research results of Lifshitz et al. (2022),[15] the semen variables after the COVID-19 vaccine have been largely inside the usual WHO reference ranges and did not alter any correlative deleterious impact from COVID-19 vaccine.

Reschini et al., (2022)[22] conducted a research on the effect of COVID-19 vaccine on male fertility in a group of infertile males from Assisted Reproductive Technologies married people in Italy. The COVID-19 vaccination had no impact on fertilization rate or sperm criteria, they revealed. That was correct just after a variety of vaccines were considered (messenger RNA or viral vector).

Safrai et al., (2021)[23] explored the role of the BNT162b2 vaccine on sperm parameters. There was no significant difference in semen volume, total sperm, or movement evaluation in men experiencing childbearing therapies before and after COVID-19 vaccination.

COVID-19 vaccines had no effect on reproductive capacity in both associates' men and women trying to fall pregnant (Wesselink et al., 2022).[27] Gonzalez et al., (2021)[7] investigated sperm variables before and after concurrent administration of a COVID-19 messenger RNA vaccine. There have been no big differences in any sperm measurement in this tiny sample of healthy males.

Gonzalez et al., (2021) [7] discovered that no males had become azoospermic after receiving the vaccine, and that at follow-up, 7 of the 8 oligospermic men would have risen sperm count to normozoospermic spectrum (median concentration, 22 million/mL [IQR, 17-25.5]), whereas one person stayed oligospermic..

In the current study, the mean sperm progressive motility (%) at baseline was (46.50 ± 5.04); after 3 months (30.0± 5.21) and after 6 months (42.5 ± 5.11), and there was a significant difference in sperm progressive movement (percentage) between variables after 3 and 6 months (p3= 0.003). There was no significant difference in sperm morphology (percentage) between variables after 3 and 6 months (p3= 0.096).

After the second vaccine dose, the median sperm concentration increased significantly to 30 million/mL (IQR, 21.5-40.5; P =.02) and the median total motile sperm count to 44 million (IQR, 27.5-98; P =.001). Both sperm volume and motility risen exponentially (Vishvkarma,Voysey et al., 2021). [25,26] The longer period of abstinence before the second sampling could explain the increase.

The impact of BNT162b messenger RNA, and the COVID-19 disease vaccine on semen quality was explored by Barda et al., (2022).[(2)] Total sperm concentration and as a whole motile count rose just after second vaccine compared to pre-vaccination specimens. The proportion of motile sperm no longer kept switching after the vaccine.

Our results showed The mean sperm DNA fragmentation (%) at baseline was (22.3 ± 4.5); after 3 months (31.5 ± 5.12) and after 6 months (18.2 ± 3.01) with statistically significant difference in sperm DNA fragmentation (%) between baseline and after 3 months (p1= 0.011).

Throughout furthermore to those other sperm parameters, Haghpanah et al., (2021)[(8)] suggested assessing the sperm deoxyribonucleic acid fragmentation index (DFI) in COVID-19 patient populations to assess male fertility. The enhanced sperm DNA fragmentation index (DFI) in COVID-19 patient populations is due to testicular inflammatory response; enhanced ROS production causes sperm deoxyribonucleic acid destruction (Anifandis et al., 2020).[(1)]

It could even be noted that the sperm characteristics after COVID-19 vaccination have been mostly within normal range variations. The findings back up the idea that the COVID-19 vaccine is reliable.

Our research has both advantages and disadvantages. Our study's resilience is that it is the first to offer information about the effect of COVID-19 vaccine on sperm variables in an Egyptian population. However, the sample size was small.

It is necessary to collect a larger and more diverse sample. Furthermore, because mRNA technology is increasingly being used to develop new vaccines to treat a variety of conditions of particular public health importance, the findings must be confirmed in long-term studies. Furthermore, there is a scarcity of information on patient serum hormones and clinical features that can influence sperm quality.

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