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Research Article

The Impact of COVID-19 Vaccines on Male Semen Parameters: A Retrospective Cohort Study

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The emergence of SARS-CoV-2 and the subsequent COVID-19 pandemic necessitated the development of adequate vaccines. Despite vaccines being demonstrated to be safe and effective for preventing severe disease and death, vaccine hesitancy remains. Reasons include concerns over adverse effects on male fertility, which have not been widely investigated. Therefore, this study is aimed at determining the impact of COVID-19 vaccination on semen parameters in a retrospective cohort study of South African males undergoing fertility assessment. The patients for this study were adult men who have previously undergone routine semen analysis for fertility assessment at Androcryos Andrology Laboratory (Johannesburg, South Africa) between March 2021 and March 2022. They also received vaccination within 3 months following a semen analysis and underwent a second semen analysis any time post-COVID-19 vaccination. From 277 records analysed, 46 patients met the inclusion criteria, receiving the Pfizer-BioNTech (BNT162b1) (63%), Johnson and Johnson (JNJ-78436735/Ad26.COV2S) (34.8%), and the AstraZeneca (AZD1222) (2.2%) vaccines. Sperm concentration significantly increased postvaccination ($P = 0.0001$), with no significant changes in semen pH, volume, total sperm count, progressive motility, normal sperm morphology, or chromatin condensation. Results were not influenced by age, type of vaccine received, and the number of days following vaccination, as depicted by multiple regression analysis. In conclusion, there is no evidence of a negative impact of COVID-19 vaccination on male semen parameters, which is consistent with the emerging literature on COVID-19 vaccination and male fertility. COVID-19 vaccinations should not be dismissed based on fear of adverse effects on male fertility parameters.

1. Introduction

Coronavirus disease 19 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, a highly infectious novel coronavirus that first emerged in Wuhan, China, in December 2019 [1]. Through human-to-human transmission, there was a rapid global spread beyond China in January 2020, which subsequently resulted in a pandemic being declared by the World Health Organisation (WHO) on the 11th of March 2020 [2]. As of the 25th of May 2022, the WHO has reported more than 520 million confirmed cases and over 6.2 million deaths, globally [3]. Furthermore, various important variants of SARS-CoV-2 (alpha, beta, gamma, delta, and omicron) have emerged that have had a significant impact on the pandemic [2].

Clinically, COVID-19 commonly presents with mild-to-moderate signs and symptoms. Common clinical features include pyrexia, a dry or productive cough, dyspnoea,

myalgia, and malaise [4]. Severe life-threating complications of COVID-19 include pneumonia, acute respiratory syndrome, and multiorgan failure, mediated in part by hyperinflammatory responses and hypoxia [5]. Although there is little evidence that SARS-CoV-2 directly gains access to the male reproductive tract, COVID-19 may cause a temporary decline in semen parameters, with testosterone levels being reduced for at least 7 months or more [6–10]. Common strategies implemented to limit the spread of the disease include restriction of movement, sociospatial distancing, wearing of masks, and sterilisation of hands and surfaces [11]. However, the novelty, transmission, and mutation rate of SARS-CoV-2 necessitated the development of a vaccine to contain the COVID-19 pandemic [12].

COVID-19 vaccines are produced in various forms, notably as viral vectors, modified viruses, viral genetic nucleic acids, and recombinant protein subunits [13, 14]. With more than 60 candidate vaccines having undergone clinical trials [14], Russia was one of the first countries to develop a recombinant adenovirus-based vaccine (Sputnik V, previously known as Gam-COVID-Vac) [15]. The UK/USA (Oxford University/Cambridge) AstraZeneca (AZD1222) vaccine was developed similarly using a recombinant nonreplicating adenovirus vector [13]. The Janssen/Johnson and Johnson vaccine (JNJ-78436735/Ad26.COV2S) also uses an adenovirus vector, based on a human double-stranded DNA used to vector the Ad26 viral gene to encode for the viral S-protein [16]. Moderna (mRNA-1273) and Pfizer-BioNTech (BNT162b1) are novel mRNA-based SARS-CoV-2 vaccines, where mRNA encoding for the S-protein is preinfused in a lipid nanoparticle [17]. These mRNA vaccines have shown excellent efficacy and safety in clinical trials, decreasing the risk of SARS-CoV-2 infection within 12 days of vaccination, with low reports of adverse effects [17]. As of the 25th of May 2022, there has been more than 11.7 billion vaccine doses administered globally [3].

The rapid development and approval of vaccines have led to numerous safety concerns by the public [14], where vaccine confidence and acceptance are critical factors for effective vaccination campaigns [18]. Although global vaccine acceptance rates generally appear to be more than 70%, low vaccine acceptance rates are reported in numerous countries [18]. In South Africa, surveys have shown acceptance rates of COVID-19 vaccines between 52% and 82%, although most reports have shown vaccine acceptance rates in South Africa were below the global average [19]. Common reasons for hesitancy in the South African population includes concerns around vaccine adverse effects, mistrust in government, and belief in conspiracies, as well as being strongly influenced by social determinants such as age, education, race, geographical location, political orientation, and employment. [19–21]. There is therefore a need to address vaccine fears and urgency, particularly around misinformation about vaccines [22, 23].

Vaccine hesitancy is also related to concerns about the short- and long-term effects on male fertility, even if no plausible biological mechanisms for negative effects have been currently identified [24]. Several fertility societies have stated that the current vaccines are unlikely to affect human fertility, however, there remains limited evidence for this conclusion, particularly in different geographical regions, including South Africa. Although some studies have found an increase in sperm parameters following COVID-19 vaccination [25, 26], other studies have found no effect on semen parameters [27–31]. However, some studies have reported a temporary decline in semen parameters postvaccination [32, 33]. Furthermore, none of these studies have yet been conducted in a South African cohort. Therefore, this study is aimed at determining the impact of COVID-19 vaccination on semen parameters in a retrospective cohort study of South African males undergoing fertility assessment.

2. Materials and Methods

2.1. Study Overview. To determine the impact of COVID-19 vaccination on male fertility, a retrospective examination of recorded semen analyses from patients attending Androcryos Andrology Laboratory (Johannesburg, South Africa) was conducted. Data was retrieved from records of male patients who underwent a semen analysis within 3 months prior to a SARS-2-CoV vaccination and underwent a subsequent semen analysis any time postvaccination.

Ethical clearance was received from the Biomedical Research Ethics Committee (Reference Number: BM21/10/32) at the University of the Western Cape, Bellville, South Africa. Permission to access patient data was subsequently obtained in writing from Mr. Petrus Loubser, the General Manager of Androcryos Andrology Laboratory.

2.2. Patients Data Inclusion and Exclusion. Patient records were included for data analysis based on the following criteria: (i) patients that had a semen analysis within 3 months prior to a recorded SARS-CoV-2 vaccination, and (ii) those same patients subsequently underwent another semen analysis at any time postvaccination. Furthermore, patients receiving any COVID-19 vaccine were included for analysis. Patient records were excluded for azoospermia, recent record of surgery, fever, illness, a positive COVID test (within 3 months of semen analysis), or undergoing any treatment for male infertility at the time of the semen analysis. No further exclusion criteria were applied due to the retrospective nature of the study design and the limited medical information available in the patient records.

Patient records at Androcryos Andrology Laboratory were screened retrospectively from the 1st of March 2021 to the 31st of March 2022. This was done by an author (L.M.) who was authorised to manage and access the patient records ethically. The total number of records retrieved, and the total number of records included and excluded were recorded, along with reasons for exclusion of records from the data analysis. The retrieved data was the anonymised and transferred into spreadsheets prepared for the statistical analysis of both descriptive and comparative data.

2.3. Variables and Data Collection. The following variables were obtained from the patient records for statistical analysis: patient age, type, and date of vaccination against SARS-CoV-2; time length (days) from initial vaccination to

pre- and postvaccination semen analysis; total time length (days) between both semen analysis samples. The primary outcomes of interest for this study are semen pH, semen volume (mL), sperm concentration (x 10^6/mL), total sperm count (10^6), progressive motility (%), total progressive motile sperm count (10^6), normal morphology (%), and chromatin condensation (%).

2.4. Semen Analysis and Chromatin Condensation. The analysis of semen parameters and chromatin condensation was performed according to the Standard Operating Procedure at Androcryos Andrology Laboratory. Semen samples were provided via masturbation after 3-7 days of abstinence. Following liquefaction at 37°C for 30 minutes, semen volume and pH were recorded. Sperm concentration was assessed after immobilizing 1 mL of a well-mixed semen sample into water at 50°C-60°C for 5 minutes. Subsequently, a drop of the immobilized semen sample was transferred to the centre of the counting chamber, and counted at the microscope at 20× magnification in duplicate. Although WHO guidelines recommend using Neubauer haemocytometer chambers, a Makler counting chamber (10 microns deep) was used to determine sperm concentration. The total sperm count was then determined by multiplying the sperm concentration by the total semen volume. Sperm progressive motility was assessed by transferring a drop of the semen sample onto a warm, unfrosted slide, and then evaluated using a phase contrast microscope at 20× magnification. Sperm morphology was assessed after Papanicolaou staining according to the strict (Tygerberg) criteria for evaluation of sperm morphology [34]. Although not part of the standard semen analysis, some patient records have chromatin condensation evaluated by the Chromomycin A3 (CMA3) stain [35]. Where available, chromatin condensation was included for data analysis. The results of patient semen analysis were interpreted according to the following thresholds for normality provided by the WHO guidelines [36]: normozoospermia (sperm concentration $\geq 15 \times 10^6$/mL, normal progressive motility $\geq 32\%$, normal morphology $\geq 4\%$), oligozoospermia (sperm concentration $< 15 \times 10^6$/mL) and teratozoospermia (normal morphology $< 4\%$).

2.5. Statistical Analysis. The distribution of data was determined by the Kolmogorov-Smirnoff test. Comparison pre- versus postvaccination was done using paired *t*-test (parametric data) or Wilcoxon test (nonparametric data). A subanalysis was conducted in patients with postvaccination date less or more than 3 months after vaccine. The 3 months were chosen as cut-off based on the length of the spermatogenesis cycle [37] and that SARS-CoV-2 induced sperm damage recovers after approximately 3 months [7]. Multiple regression analysis was conducted to control for patient age, type of vaccine received, and number of days for the postvaccine semen analysis. For variables which did not show any significant difference, a retrospective sample size calculation was performed based on the comparison of two means [38]. Statistical analysis was conducted using MedCalc statistical software (Version v20.109, Mariakerke, Belgium), with a P value of <0.05 being statistically significant.

3. Results

A total of 277 records of patients were retrospectively screened to identify those meeting the inclusion criteria. Of these, 231 records were excluded, with 46 patient records subsequently included in the study. Reasons for exclusion are summarized in Figure 1. Descriptive statistics are provided in Table 1. The majority of patients received the Pfizer-BioNTech (BNT162b1) vaccine (63%), followed by the Johnson and Johnson (JNJ-78436735/Ad26.COV2S) (34.8%), and AstraZeneca (AZD1222) (2.2%) vaccines (Table 1).

According to the WHO criteria [36], patients were categorised as normozoospermic, oligozoospermic, and/or teratozoospermic (Table 1). Before and after vaccination, the percentage of patients with normozoospermia or oligozoospermia did not vary significantly in the cohort. Only 38 out of 46 (82.6%) patients underwent a sperm morphology assessment, as 8 patients had too low sperm concentration for adequate assessment. Teratozoospermia was identified in 36.8% ($n = 14$) of patients in both the pre- and postvaccination semen analysis. Based on WHO cut-off value of 32% for normal progressive motility [36], 19.5% ($n = 9$) and 26.1% ($n = 12$) of patients showed reduced progressive motility (<32%) pre- and postvaccination, respectively. In the full cohort, the mean and median for semen pH, semen volume, sperm concentration, and progressive motility were within normal parameters as outlined by the WHO [36] (Table 2). However, the mean and median for normal morphology were below the recommended threshold of 4% [36] (Table 2).

3.1. Semen Parameters Pre- and Postvaccination in the Full Cohort. Comparative statistics for the semen analysis variables pre- and postvaccination are summarized in Table 2. In the full cohort, sperm concentration significantly ($P = 0.0001$) increased postvaccination. A decrease in sperm volume and total sperm count was observed after vaccination; however, this was statistically insignificant. In addition, no significant difference was observed for length of abstinence, semen pH, progressive motility, and total progressive motile sperm count before and after vaccination. In 38 patients analysed for sperm morphology, no difference was observed pre- and postvaccination. Results for chromatin condensation were available for only 13 patients included in the study, and although there was an increase postvaccination, this was statistically not significant (Table 2). Following multiple regression analysis, we excluded any influence of age, type of vaccine received, and number of days following vaccination on the outcomes observed.

A retrospective sample size calculation was conducted to determine the minimum number of patients needed in order for the difference between the groups obtained in the results to reach statistical significance. This analysis suggested that an unrealistically large number of patients would need to be included in the study to observe any significant difference in semen volume ($n = 1{,}702$), total sperm count ($n = 17{,}384$), progressive motility ($n = 1{,}510$), total progressive motile sperm count ($n = 12{,}286$), morphology ($n = 8{,}558$), and chromatin condensation ($n = 266$) based on the differences between the groups.

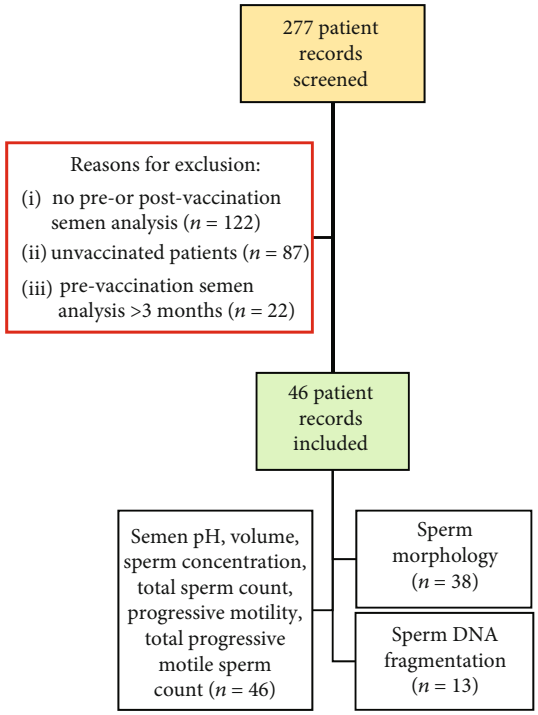

Figure 1: Flow diagram illustrating the number of patient records screened, reasons for exclusion, and final number of patients for inclusion and data analysis.

3.2. Subanalysis: Semen Analysis 3 Months following Vaccination. The full cohort was subdivided into two groups based on the timing of the postvaccination semen analysis: (i) semen analysis within 3 months following vaccination ($n = 15$; 32.6%), and (ii) semen analysis performed more than 3 months following vaccination ($n = 31$; 67.4%). For the semen analysis subgroup within 3 months following vaccination, the mean ± SD for the number of days between 1st vaccination and the semen analysis was 50.9 ± 24.5, with a range of 10–87 days. For the semen analysis subgroup of more than 3 months following vaccination, the mean ± SD for the number of days between 1st vaccination and the semen analysis was 138 days ± 29.8 days, with a range of 93–217 days. Sperm concentration increased nonsignificantly in those patients who had semen analysis within 3 months following vaccination ($P = 0.4212$). However, this was significant ($P < 0.0001$) in those patients who had a semen analysis of more than 3 months following vaccination. There were no statistical differences in these postvaccination subgroups when compared to prevaccination data for semen pH ($P = 0.1272$ and $P = 0.5212$, respectively), sperm volume ($P = 0.1058$ and $P = 0.4124$, respectively), total sperm count ($P = 0.0554$ and $P = 0.3272$, respectively), progressive motility ($P = 0.3457$ and $P = 0.2099$, respectively), total progressive motile sperm count ($P = 0.2078$ and $P = 0.5566$, respectively), sperm morphology ($P = 0.9987$; $n = 13$ and $P = 0.3951$; $n = 25$, respectively), or chromatin condensation ($P = 0.0704$; $n = 2$ and $P = 0.1432$; $n = 11$, respectively).

4. Discussion

In South Africa, COVID-19 vaccine acceptance rates are below the global average [19], and there is a local and global need to address vaccine fears and misinformation [22, 23]. Globally, vaccine hesitancy concerns have been raised over potential negative effects on both male and female fertility [39, 40]. The results of this retrospective study identified 46 patients who had received a COVID-19 vaccine within 3 months of a semen analysis (prevaccination), and subsequently underwent another semen analysis anytime postvaccination. No significant differences were identified pre- and postvaccination for semen pH, volume, progressive motility, normal morphology, and SDF. However, sperm concentration was found to be significantly increased postvaccination, with no significant difference for total sperm count.

There are numerous forms of COVID-19 vaccines, including vaccines based on use of viral vectors, modified viruses, genetic (nucleic acids), and recombinant protein subunits [13, 14]. In our study, 63% of participants used BNT162b1 vaccine. The Pfizer-BioNTech (BNT162b1) is based on novel mRNA-technology, and therefore not using whole viruses or viral components [17]. JNJ-78436735/Ad26.COV2S was used by 34% of patients included in this study, which is an adenovirus vector based on a human double-stranded DNA to vector the Ad26 viral gene that then encodes for the S-protein [16]. AZD1222 was used by 2.2% of patients, which is also based on the use of recombinant nonreplicating adenovirus vectors [13].

Interestingly, our results suggest an increase in sperm concentration with COVID-19 vaccine (Table 2). Similarly, the BNT162b2 and mRNA-1273 vaccines significantly increased semen volume, sperm concentration, total sperm motility, and total motile sperm count in 45 healthy males [25]. In 101 men, where 76% received mRNA vaccines, 20% viral vector vaccines, and 2% a mixed formulation, sperm concentration, total sperm count, and progressive motility increased postvaccination, although semen volume decreased [26]. Furthermore, we found the increase in sperm concentration was significant only for postvaccination semen analysis more than 3 months following vaccination. However, this percentage of change is within normal human variation of semen parameters in individuals, especially for sperm concentration [41], and is not likely to be directly due to vaccine exposure [25].

Numerous studies have found no effect of various COVID-19 vaccines on male fertility, which is consistent with the results of our study with the exception of sperm concentration. Low rates of reduced semen parameters were reported in 75 fertile males between 1 and 2 months following a second dose of BNT162b2 vaccine [28]. In 72 male patients undergoing IVF treatment post-BNT162b2 vaccination, a comparison of records prior to vaccination were compared with the post-vaccination samples, finding no difference in semen volume, sperm concentration, and total motile sperm count [30]. In a retrospective study of 106 men of couples undergoing assisted reproduction technology procedures, there was no change in semen parameters or fertilisation rate before and after COVID-19 vaccination,

Table 1: Descriptive statistics of the cohort ($n = 46$).

Variables	Mean ± SD
Age (years)	38.0 ± 5.5
Days between vaccination and pre-semen analysis	45.2 ± 27.7
Days between vaccination and post-semen analysis	110.3 ± 50.1
Days between pre and post-semen analysis	155.4 ± 53.9
Vaccine received	***n*(%)**
Pfizer-BioNTech (BNT162b1)	29 (63.0%)
Johnson and Johnson (JNJ-78436735/Ad26.COV2S)	16 (34.8%)
AstraZeneca (AZD1222)	1 (2.2%)
Semen analysis abnormalities	***n*(%)**
Patients with normozoospermia[†] (prevaccination)	15 (32,6%)
Patients with normozoospermia[†] (postvaccination)	14 (30.4%)
Patients with oligozoospermia[‡] (prevaccination)	14 (30.4%)
Patients with oligozoospermia[‡] (postvaccination)	10 (21.7%)
Patients with progressive motility <32% (prevaccination)	9 (19.5%)
Patients with progressive motility <32% (postvaccination)	12 (26.1%)
Patients with teratozoospermia[§] (prevaccination) ($n = 38$)	14 (36.8%)
Patients with teratozoospermia[§] (postvaccination) ($n = 38$)	14 (36.8%)

[†]Normozoospermia = Sperm concentration ≥ 15 x 10 6/mL, Progressive motility ≥ 32 %, and normal morphology ≥ 4 %; [‡]Oligozoospermia = Sperm concentration < 15 x 10 6/ mL; [§]Teratozoospermia = Normal sperm morphology < 4 %.

which included the BNT162b2 (69%), mRNA-1273 (19%), AZD1222 (9%), and JNJ-78436735/Ad26.COV2S (1%) vaccines [29]. Furthermore, 43 semen samples from a human sperm bank analysed before and after an inactivated COVID-19 vaccine found no significant changes in semen volume, sperm concentration, progressive motility, and total progressive motile count after the second dose [31].

There have been some suggestions of a negative effect of vaccination on semen parameters in 2 studies, although this was temporary [33] or lacks any clinical impact [32]. In 60 healthy males with previous normal semen analyses prior to BNT162b2 vaccination, no difference for semen pH, semen volume, sperm concentration, or morphology was found, although there was a small but statistically significant reduction in total and progressive motility. However, all values remained within normal limits according to WHO guidelines, and are regarded as clinically insignificant by the authors [32]. In a retrospective study, Gat et al. [33] reported a temporary impairment in sperm concentration and total motile count in 37 patients who received the BNT162b2 vaccine; however, there were no significant changes in semen volume and sperm motility [33].

The results from this study, alongside the majority of the current evidence from similar studies, do not show any evidence for COVID-19 vaccines to negatively impact semen parameters [25, 28–31]. This is further supported by Wesselink et al. [42], reporting that vaccination against COVID-19 did not reduce male or female fecundability ratio (FR). This is in contrast to COVID-19 disease which was found to reduce male, but not female, fecundability ratio [42]. Furthermore, there appears to be a significantly decreased risk of developing orchitis and/or epididymitis in males following COVID-19 vaccination when compared to matched males who did not receive a vaccination [43].

Limited research conducted on non-COVID-19 vaccines seems to further exclude any possible negative impact of vaccination on male fertility. For example, no association was found between smallpox vaccination and subsequent male infertility diagnosis in a retrospective study of more than 250,000 US Military personnel [44]. Similarly, the administration of the anthrax vaccine had no negative effect on semen parameters, fertilization rate, embryo quality, or clinical pregnancy rates in male partners of couples who were undergoing assisted reproduction [45]. Furthermore, vaccination against the human papilloma virus (HPV) may prevent cases of male infertility, as HPV presence in semen is known to negatively affect fertility [46]. In males with HPV-induced infertility, the administration of the HPV vaccine may improve semen parameters, and reduce relapse of infection with persistent HPV in semen [46]. In male rats, the HPV vaccine has no detrimental effects on male fertility parameters, including histomorphology of testes and epididymis, sperm count, and sperm motility [47].

Although there are relatively limited studies investigating SARS-CoV-2 infection in male reproduction, the current data available shows no significant evidence for the presence of viral RNA in semen [6, 8, 10]. However, the current evidence does suggest that SARS-CoV-2 infection may negatively affect seminal parameters and reduce testosterone levels, particularly in males with more severe febrile illness [6, 8, 10]. With little evidence that the virus is present in male reproductive tissues during or postinfection, any negative effect on male fertility parameters is suggested to be mediated by nonspecific mechanisms. This includes changes

Table 2: Comparison of semen analysis parameters pre- and postvaccination for the full cohort.

Variable	Semen sample (pre-/postvaccination)	n	Mean ± SD	Median (IQR)	P value
Abstinence period (days)	Pre	46	4.2 ± 1.0	4.0 (3.0–5.0)	0.3810∗
	Post	46	4.4 ± 1.4	4.0 (3.0–5.0)	
Semen pH	Pre	46	7.5 ± 0.2	7.5 (7.5–7.6)	0.1581∗
	Post	46	7.5 ± 0.2	7.5 (7.3–7.7)	
Semen volume (mL)	Pre	46	3.0 ± 1.2	2.7 (2.2–3.9)	0.0905^{+}
	Post	46	2.8 ± 1.7	2.5 (1.8–3.6)	
Sperm concentration (10^6/mL)	Pre	46	36.9 ± 35.9	25.0 (6.5–62.0)	**0.0001**∗
	Post	46	41.1 ± 40.3	25.5 (7.0–79.0)	
Total sperm count (10^6)	Pre	46	112.8 ± 120.9	74.6 (14.3–159.6)	0.0538∗
	Post	46	107.5 ± 128.4	65.6 (10.8–124.0)	
Progressive motility (%)	Pre	46	43.3 ± 13.6	45.0 (35.0–50.0)	0.1106^{+}
	Post	46	41.3 ± 14.1	50.0 (30.0–50.0)	
Total progressive motile sperm count (10^6)	Pre	46	57.0 ± 67.5	31.0 (4.3–90.5)	0.2402∗
	Post	46	53.6 ± 67.0	24.9 (5.0–72.9)	
Normal sperm morphology (%)	Pre	38	3.5 ± 1.7	3.0 (2.0–5.0)	0.4912^{+}
	Post	38	3.4 ± 1.6	3.0 (2.0–4.0)	
Sperm chromatin condensation (%)	Pre	13	40.2 ± 16.8	40.0 (27.3–49.0)	0.0662^{+}
	Post	13	46.7 ± 20.6	39.0 (34.5–63.5)	

$^{+}$ Parametric statistical comparison done with paired t-test; ∗ Nonparametric comparison done with Wilcoxon test; Bold indicates $P < 0.005$;.

to testicular function, inflammatory cell infiltration into reproductive tissues, systemic inflammation and pyrexia, and the potential of the virus to incorporate genetic material into the germ cell genome [48–50]. Furthermore, autopsy analysis of testicular tissues has revealed significant damage to testicular histology in patients who died from COVID-19 [10]. Therefore, the current evidence suggests that there is a greater potential for SARS-CoV-2 infection to disrupt male fertility parameters than receiving a COVID-19 vaccination.

This study has numerous limitations. As a retrospective study with the use of convenience sampling, it is prone to selection bias. To limit this bias, only records available during a predetermined time period were considered, and the total number of records, as well as the number of included and excluded records, are reported. The included patients in this study have an unknown fertility status, limiting the generalisability of the results. The study also did not include a case-control cohort, using intragroup statistical analysis only. There was a relatively low sample size of patients that met the inclusion criteria, which may limit the generalisability of the results. However, the retrospective sample size analysis suggested that an unrealistically large number of patients should be analysed to observe any significant statistical difference in all parameters investigated. Although chromatin condensation was included in the outcomes of the study, there were limited patient records for this

parameter pre- and postvaccination to draw appropriate conclusions, and no measure of seminal oxidative stress was available. Furthermore, the study included patients receiving 3 different vaccines which have been investigated in the same cohort. However, following multiple regression analysis for the types of vaccines, there was no significant impact of the type of vaccines on the results.

5. Conclusion

The study shows that COVID-19 vaccination does not negatively impact semen parameters in a South African male patients undergoing semen analysis. This supports emerging evidence that COVID-19 vaccines do not affect male fertility. As SARS-CoV-2 infection may disrupt semen parameters in males with moderate-to-severe infection, vaccination appears to have a lower risk of fertility impairment in men compared to COVID-19. Therefore, COVID-19 vaccinations should not be dismissed based on fear of adverse effects on male fertility parameters.

Data Availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Additional Points

Practitioner Points. (1) Vaccination against COVID-19 does not negatively affect semen parameters. (2) This is not influenced by patient age, type of vaccine received, or the number of days following vaccination. (3) COVID-19 vaccinations should not be dismissed based on fear of adverse effects on male fertility parameters.

Ethical Approval

The authors confirm that the ethical clearance was received from the Biomedical Research Ethics Committee (Reference Number: BM21/10/32) at the University of the Western Cape, Bellville, South Africa.

Disclosure

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The content hereof is the sole responsibility of the authors and do not necessarily represent the official views of the SAMRC or the funders.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

All authors are responsible for the conceptualization, study design, methodology, review, and editing of the manuscript. L.M. is responsible for patient file screening, eligibility, and data extraction. R.F., K.L., and R.H. are responsible for statistical analysis. K.L. and R.F. are responsible for drafting the original manuscript. All authors agree to be accountable for all aspects of work ensuring integrity and accuracy. Kristian Leisegang and Renata Finelli are co-lead authors.

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