ORIGINAL ARTICLES

Effect Of Female Covid-19 Inactivated Vaccination Doses on Cycle Outcome of Artificial Insemination with Husband Semen

Yating Sun, Luyun Zhang, Yao Jia, Jia Wang, Aizhen Zhu*

Background: *This study aimed to investigate the impact of different doses of COVID-19 inactivated vaccine on female fertility.*

Materials and Methods: *A total of 595 assisted insemination with husband's sperm (AIH) cycles were retrospectively analyzed in this cohort study. The participants were divided into three groups: the unvaccinated group, the 1 or 2 doses group, and the 3 doses group based on their COVID-19 vaccination status prior to insemination. Reproductive outcomes, including biochemical pregnancy, clinical pregnancy, ongoing pregnancy, and live birth, were assessed across the three groups.*

Results: *The analysis revealed no significant differences in reproductive outcomes among the three groups. The rates of biochemical pregnancy, clinical pregnancy, ongoing pregnancy, and live birth were comparable among the unvaccinated group, the 1 or 2 doses group, and the 3 doses group (P=0.369, P=0.975, P=0.686, and P=0.441, respectively). The Multivariate logistic regression analysis indicated that the doses of COVID-19 inactivated vaccine did not independently impact the reproductive outcomes of AIH cycles.*

Conclusion: *The findings suggest that the doses of COVID-19 inactivated vaccine do not have a detrimental effect on female fertility in AIH cycles.*

BACKGROUND

Inactivated vaccine was the most commonly used in China.[1] Based on our understanding of the immune response of inactivated vaccines and the efficacy and safety data from clinical trials, current guidelines from organizations around the world did not restrict the use of COVID-19 inactivated vaccines for couples who planned to become pregnant or planned to become pregnant with ART.[2-6] However, infertile couples were still concerned about whether the vaccination would affect the ART outcome. Artificial insemination with husband sperm (AIH) involves the preparation of sperm from husband and artificially inseminates into the partner's uterus around ovulation. This is a relatively natural fertilization process compared to in vitro fertilization embryo transfer (IVF-ET).[7,8] Previous research had demonstrated that factors such as receiving the COVID-19 inactivated vaccine, the dosage administered, and the time interval between vaccination and assisted insemination with husband's sperm (AIH) did not influence the outcomes of AIH.[1,9] However, they did not compare the clinical outcome of unvaccinated group before fertilization and vaccinated groups with different doses before fertilization. The aim of this retrospective cohort study was to investigate the

Department of reproductive medicine, Yuncheng central hospital, Yuncheng, Shanxi, China.
Address for correspondence to: Aizhen Zhu, BA, Department of reproductive medicine, Yuncheng central hospital, Yuncheng, Shanxi, China.
(zhuaizhen8768@163.com). Mobile no: 13835968768.
Financial Disclosures: This work was supported by Scientific Research Project of Shanxi Provincial Health Commission (No. 2023064).

association between the doses of COVID-19 inactivated vaccine received by women and the outcomes of assisted insemination with husband's sperm (AIH), with unvaccinated cycles serving as the reference group.

MATERIALS AND METHODS

Patients and Methods

The retrospectively cohort study was carried out at the Department of Reproductive Medicine, Yuncheng Central Hospital of Shanxi Province (Shanxi, China). Couples receiving AIH treatment between January 2021 and December 2022 were included in the study.

Inclusion criteria included: (1) Infertility period ≥1 year; (2) Normal uterine cavity, and at least one fallopian tube is unblocked (confirmed by hysterosalpingography or laparoscopy)

The exclusion criteria were as follows: (1) The cycle was cancelled due to non-dominant follicles after treatment or the total motile sperm count (TMSC) after processing was less than 10*106;

(2) No response; (3) Receiving non-inactivated vaccines or unknown vaccines; (4) Endometrial thickness less than 7mm on the day of insemination; (5) Abstinence days outside of 2 to 7 days.

493 couples (667 cycles) were treated with AIH. These couples were further screened according to the above exclusion criteria. Finally, 595 cycles (438 couples) were included in the study and were divided into two groups. The unvaccinated group (344 cycles, 253 couples) included women who were not vaccinated or were vaccinated after insemination. The vaccinated group (251 cycles, 185 couples) included women who were vaccinated prior to insemination and was subdivided into 2 subgroups by vaccination doses. The 1 or 2 doses group (146 cycles, 108 couples) included women who received 1 or 2 doses of the vaccine. The 3 doses group (105 cycles, 77 couples) included women who received 3 doses of the vaccine. (Figure 1)

Figure :1

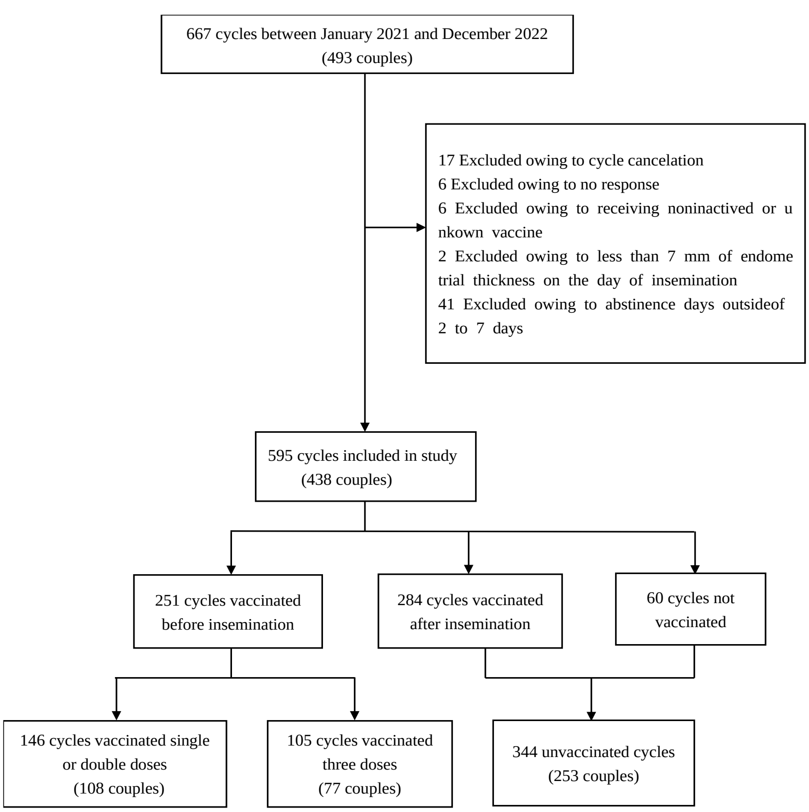

FIGURE 1
Study flowchart

We followed up enrolled couples with vaccination information by telephone. Baseline clinical features and reproductive outcome data were collected from the Department of Reproductive Medicine database. Patient general information such as female ag, male age, female body mass index (BMI), Antral follicular count (AFC), Gravidity, Parity, Miscarriage, Ectopic, type of infertility, infertility duration, infertility factors, cycle number, treatment cycle type, dominant follicle number, endometrial thickness on the day of insemination, abstinence duration, total motile sperm count (TMSC) after processing were recorded.

This study was approved by the Ethics Committee of Yuncheng Central Hospital of Shanxi Province. (No. YXLL2023009).

AIH protocol

Natural cycle: From the 8th to 10th day of the menstrual cycle, vaginal B-ultrasound was used to monitor follicle development and endometrial thickness and blood luteinizing hormone (LH), estradiol (E2) and progesterone (P) values were monitored at the same time. If a spontaneous LH peak (more than 3 times higher than the basal LH) occurred, the follicle diameter was ≥18mm, and the serum E2 level reached an average of 180~250pg /ml per mature follicle, AIH would be performed within 24 hours. If there was no LH peak, follicle diameter was ≥18mm and serum E2 level reached an average of 180~250pg /ml per mature follicle, AIH was performed within 36 hours after HCG5000~10000IU. AIH could also be performed immediately after HCG injection and B ultrasound confirmation of ovulation.

COS: On the 3rd to 5th day of menstruation, B ultrasound was used to evaluate the endometrial thickness, monitor the number of AFC, and patients were given letrozole (LE; Jiangsu Hengrui) 2.5~5 mg, once a day for 5 days. The development of follicles and endometrial thickness were monitored by B-ultrasound starting from the 10th day of the menstrual cycle, meanwhile the serum LH, E2 and P levels were monitored. When the diameter of the dominant follicle was ≥18 mm and the serum E2 level reached an average of 180~250pg/ml per mature follicle, HCG was given 5 000~10 000 U (Zhuhai Lizhu), and AIH was administered within 36 h.

Sperm processing: The husband was instructed to abstain from sex for 2~7 days before sperm extraction. Sperm was extracted by masturbation and was optimized by density gradient centrifugation. 15 ml conical centrifuge tube (Falcon, USA) were added with 1.0 ml 80% gradient solution, an equal amount of 40% gradient solution was slowly added to the top of the gradient solution, then fully liquefied sperm was slowly added to the top of the gradient solution. The supernatant in the conical tube was discarded after centrifuging 300 g for 20 min, leaving a little precipitation. A gametic buffer (GB; Cook, Australia) was added to another 15ml conical centrifuge tube, the precipitation was added into a centrifuge tube containing GB. Discard the supernatant and leave about 0.5 ml of the precipitation for mixing after centrifuging 200 g for 5 min. The sperm concentration and motility were observed by makler plate, and the TMSC after processing was calculated

Intrauterine insemination: Female patient was instructed to empty the bladder and was scrubed the vulva with sterile saline. The surgeon opened the vagina with a speculum, scrubbed the vagina with sterile saline. 0.5 ml of sperm was slowly injected into the uterine cavity using the artificial insemination tube (Shenzhen Huan Ho).

Luteal support and pregnancy judgment: Take progesterone capsule (Zhejiang Xianju) orally 200 mg/d after ovulation. For patients with low estrogen levels before ovulation, oral supplementation of estradiol valerate tablets (Guangzhou Baier) 1 to 2 mg once a day could be done. After the pregnancy was confirmed by blood β-HCG positive test 14 to 16 days after surgery, the drug was continued to be used until 8 to 10 weeks of pregnancy.

The primary outcome indicator of this study was live birth (live delivery at 28 weeks of gestation or above), and the secondary outcome indicators included biochemical pregnancy (serum β-HCG level was greater than 10 mIU/ml on 14 to 16 days after surgery), clinical pregnancy (visible pregnancy capsule by ultrasound examination on 35 days after Surgical, including ectopic pregnancy) and ongoing pregnancy (intrauterine pregnancy of more than 12 weeks confirmed by vaginal ultrasound).

Statistical analysis

SPSS 26.0 software (IBM) was used for statistical analysis. The continuous variables did not conform to the normal distribution after testing by the Shapiro Wilk (S-W) method, were expressed as the median (25th percentile, 75th percentile) [M (P25, P75)], and Kruscarl-Wallis H(K-W) test was used for comparison among groups. Categorical variables were expressed as frequency or rate, and comparisons among groups were made using Pearson's chi-square test or Fisher's exact test. The biochemical pregnancy rate, clinical pregnancy rate, ongoing pregnancy rate and live birth rate among different vaccine dose groups were compared. Then a multivariate logistic analysis regression model was performed using unvaccinated cycles as the reference, the adjusted risk ratio (RR) and 95% confidence interval (CI) were calculated for biochemical pregnancy, clinical pregnancy, ongoing pregnancy and live birth. Next, a generalized estimating equation (GEE) was used to examine the relationship between individual factors and ongoing pregnancy, controlling for multiple cycles within the same couple. RR and 95% CI were calculated for candidate factors. Two-tailed $P<0.05$ was considered statistically significant.

RESULTS

From January 2021 to December 2022, data from 595 AIH cycles (438 couples) were included in our study. The vaccination coverage rate of female seeking for AIH treatment was 42.2% (251/595). In the female vaccinated group, there were 146 cycles in 1 or 2 doses group and 105 cycles in 3 doses group. Table 1 summarizes demographic Characteristics and vaccination status per artificial insemination cycles with husband sperm stratified by vaccination doses prior to insemination. There were statistically significant differences in the female age, male age, female BMI, infertility duration, infertility factors and female partner vaccination dose in three different female vaccination dose groups ($P<0.05$). Another characteristics and vaccination status did not differ significantly ($P>0.05$).

Table 2 shows the frequencies for reproductive outcome of artificial insemination with husband sperm stratified by vaccination doses prior to insemination. The analysis revealed no significant differences in reproductive outcomes among the three groups. The rates of biochemical pregnancy were 24.1% in the unvaccinated group, 20.5% in the 1 or 2 doses group, and 18.1% in the 3 doses group ($P=0.369$). The rates of clinical pregnancy were 18.9% in the unvaccinated group, 19.2% in the 1 or 2 doses group, and 18.1% in the 3 doses group ($P=0.975$). The rates of ongoing pregnancy were 16.9% in the unvaccinated group, 16.4% in the 1 or 2 doses group, and 13.3% in the 3 doses group ($P=0.686$).

The rates of live birth were 16.6% in the unvaccinated group, 15.8% in the 1 or 2 doses group, and 11.4% in the 3 doses group ($P=0.441$). Multivariate logistic regression analysis indicated that the doses of COVID-19 inactivated vaccine did not independently impact the on female fertility in AIH cycles after adjusted for female age, female BMI, total antral follicle count (AFC), infertility factors, treatment cycle type, dominant follicle number, endometrial thickness on the day of insemination, TMSC after processing [Adjusted RR(95%CI) 0.879(0.540-1.431) in 1 or 2 doses group, 0.737(0.411-1.323) in 3 doses group for biochemical pregnancy rate;

Adjusted RR (95%CI) 1.112(0.667-1.855) in 1 or 2 doses group, 0.969(0.532-1.767) in 3 doses group for clinical pregnancy rate; Adjusted RR (95%CI) 1.079(0.626-1.858) in 1 or 2 doses group,0.748(0.383-1.461) in 3 doses group for ongoing pregnancy rate; Adjusted RR (95%CI) 1.052(0.607-1.824) in 1 or 2 doses group, 0.653(0.324-1.317) in 3 doses group for live birth].

The predictors in the GEE model for live birth were presented in Table 3. After controlling bias from multiple cycles within the same couple, female COVID-19 vaccine dose did not to predict the live birth of AIH cycles. The independent influence factor to predict live birth of AIH cycles was treatment cycle type.

Table1: Demographic Characteristics and vaccination status per artificial insemination cycles with husband sperm stratified by vaccination doses prior to insemination.

Variables	Unvaccinated group	Vaccinated group		*P* value
		1 or 2 doses	3 doses	
No. of cycles	344	146	105	
Female age, median (IQR), y	28(26,30)	29(27,32)	29(27,31)	0.005
male age, median (IQR), y	29(27,31)	30(28,32)	30(28,33)	0
Female BMI, median (IQR), kg/m²	22.6(20.2,25.48)	22.2(20.68,25.73)	23.9(21.05,26.4)	0.022
Total antral follicle count（AFC）	17(12,24)	16.5(12,20.3)	16(11,23)	0.105
Gravidity, n (%)				0.853
0	244(70.9)	102(69.9)	75(71.4)	
1	66(19.2)	31(21.2)	23(21.9)	
≥2	34(9.9)	13(8.9)	7(6.7)	
Parity, n (%)				0.726#
0	308(89.5)	134(91.8)	92(87.6)	
1	35(10.2)	11(7.5)	12(11.4)	
≥2	1(0.3)	1(0.7)	1(1.0)	
Miscarriage, n (%)				0.098
0	264(76.7)	111(76.0)	90(85.7)	
1	66(19.2)	24(16.4)	13(12.4)	
≥2	14(4.1)	11(7.5)	2(1.9)	
Ectopic, n (%)				0.192#
0	341(99.1)	146(100.0)	105(100.0)	
1	3(0.9)	0(0.0)	0(0.0)	
Type of Infertility, n (%)				0.87
Primary	261(75.9)	110(75.3)	77(73.3)	
Secondary	83(24.1)	36(24.7)	28(26.7)	
Infertility duration, median (IQR), y	3(2, 4)	2(2, 3)	3(1.5, 4)	0.001
Infertility factors, n (%)				0.002
Pelvic -tubal factor	69(20.1)	21(14.4)	8(7.6)	
Ovulation disorders and low ovarian reserve	159(46.2)	57(39.0)	47(44.8)	
Male factor	32(9.2)	12(8.2)	7(6.7)	
Others	84(24.4)	56(38.4)	43(41.0)	
Cycle number, n (%)				0.997#
1	253(73.5)	108(74.0)	77(73.3)	
2	81(23.5)	33(22.6)	25(23.8)	
≥3	10(2.9)	5(3.4)	3(2.9)	
Treatment cycle type, n (%)				0.32
Natual	37(10.8)	17(11.6)	17(16.2)	
COS	307(89.2)	129(88.4)	88(83.8)	
Dominant follicle number, n (%)				0.649
1	282(82.0)	124(84.9)	89(84.8)	
2	62(18.0)	22(15.1)	16(15.2)	
Endometrial thickness on the day of insemination, median (IQR), mm	10(8.5,11)	9.55(8.45,10.85)	9.3(8.4,10.8)	0.757
Abstinence duration, Median (IQR), y	3(3,4)	3(3,5)	4(3,5)	0.395
TMSC after processing, median (IQR),10^6	24(16,34)	24(12.56,36)	24(16,30)	0.639
female partner doses of vaccination, n (%)				0
0	321(93.3)	8(5.5)	0(0.0)	
1 or 2	18(5.2)	116(79.5)	15(14.3)	
3	5(1.5)	22(15.1)	90(85.7)	
Female interval between the last dose and insemination, n (%)				0.51
＜3 months	/	13(8.9)	12(11.4)	
≥3 months	/	133(91.1)	93(88.6)	
Male interval between the last dose and insemination, n (%)				0.003
＜3 months	8(34.8）	15(10.9)	10(9.5)	
≥3 months	15(65.2)	123(89.1)	95(90.5)	

Fisher exact test was used.

Table2: Reproductive outcome of artificial insemination with husband sperm stratified by vaccination doses prior to insemination.

Variables	Unvaccinated group	Vaccinated group		*P* value
		1 or 2 doses	3 doses	
Biochemical pregnancy, %(n)	24.1(83/344)	20.5(30/146)	18.1(19/105)	0.369#
Adjusted RR (95%CI)	ref.	0.879 (0.540-1.431)	0.737 (0.411-1.323)	
Adjusted *P* value	/	0.604	0.307	0.572*
Clinical pregnancy, %(n)	18.9(65/344)	19.2(28/146)	18.1(19/105)	0.975#
Adjusted RR (95%CI)	ref.	1.112 (0.667-1.855)	0.969 (0.532-1.767)	
Adjusted *P* value	/	0.683	0.919	0.897*
Ongoing pregnancy, %(n)	16.9(58/344)	16.4(24/146)	13.3(14/105)	0.686#
Adjusted RR (95%CI)	ref.	1.079 (0.626-1.858)	0.748 (0.383-1.461)	
Adjusted *P* value	/	0.784	0.395	0.612*
live birth, %(n)	16.6(57/344)	15.8(23/146)	11.4(12/105)	0.441#
Adjusted RR (95%CI)	ref.	1.052 (0.607-1.824)	0.653 (0.324-1.317)	
Adjusted *P* value	/	0.856	0.234	0.437*

#Reproductive outcome difference in three different vaccination dose groups before adjustment.
*Reproductive outcome difference in three different vaccination dose groups after adjustment.

Table 3: Adjusted binary logistic regression model for predictors of live birth of artificial insemination with husband sperm using generalized estimating equations.

Factors	Adjusted RR (95%CI)	*P*-value
female vaccination doses prior to insemination		
0	ref.	
1 or 2	1.152(0.322-4.123)	0.827
3	0.349(0.079-1.553)	0.167
female partner vaccination doses prior to insemination		
0	ref.	
1 or 2	0.759(0.208-2.771)	0.676
3	2.121(0.518-8.690)	0.296
Female age, y	0.928(0.858-1.003)	0.061
Female BMI, kg/m^2	1.069(0.995-1.147)	0.067
Total antral follicle count（AFC）	1.025(0.980-1.072)	0.287
Infertility factors		
Pelvic -tubal factor	ref.	
Ovulation disorders and low ovarian reserve	1.148(0.561-2.352)	0.705
Male factor	0.411(0.100-1.690)	0.218
Others	0.905(0.431-1.901)	0.792
Treatment cycle type		
Natual	ref.	
COS	4.318(1.093-17.054)	0.037
Dominant follicle number		
1	ref.	
2	1.527(0.852-2.734)	0.155
Endometrial thickness on the day of insemination, mm	1.042(0.918-1.183)	0.525
TMSC after processing, median, 10^6	0.995(0.977-1.013)	0.560

DISCUSSION

The objective of this study was to assess the impact of COVID-19 inactivated vaccine doses on female fertility, with a focus on assisted insemination with husband's sperm (AIH) clinical outcomes. The results indicated that there was no significant effect observed on AIH clinical outcomes. COVID-19 vaccines mainly include inactivated virus vaccine, viral vector vaccine, and mRNA vaccine. Inactivated vaccine is physically or chemically inactivated, but retains the integrity of the virus particles, using the entire virus as a vaccine target. The targeted immune response of inactivated vaccines is usually humoral and cellular, with almost no reactivity, and therefore has a high safety.[10] Given that the COVID-19 inactivated vaccine is widely utilized in China, experts in reproductive medicine should take into account its potential impact on reproduction. Initial studies have indicated that there is no link between COVID-19 inactivated vaccines and fertility rates.[11,12] Existing research had also focused on whether pregnancy need to be delayed after COVID-19 inactivated vaccination and the optimal interval to delay pregnancy.[13] Several studies have investigated the potential sperm toxicity of the COVID-19 inactivated vaccine in men. The findings revealed that receiving the COVID-19 inactivated vaccine did not adversely affect various male sperm parameters, such as sperm volume, sperm concentration, total sperm count, forward motility sperm count, sperm morphology, and sperm DNA fragmentation index.[14-17] Wang et al.[9] collected clinical data from 4185 couples who received the first AIH treatment at 10 centers in 9 provinces in China from July 2021 to February 2022 and followed up the vaccination status of both men and women, showing that whether the woman or the man received the vaccine, the type of vaccination and the interval between vaccination and AIH did not affected the success rate of artificial insemination. Another retrospective cohort study in 2022 included 492 women who underwent artificial insemination with husband sperm (AIH) (725 cycles), it was found that whether women were vaccinated with COVID-19 inactivated vaccine, one dose of vaccine and two or more doses of vaccine before fertilization and the time interval between the last vaccination and AIH had no adverse effects on fertility in AIH cycle[1]. However, existing studies had not compared the clinical outcome of the group that was not vaccinated before fertilization with the group that was vaccinated with different doses.

AIH is an effective method to study the influence of one factor on implantation. On the one hand, its fertilization process is relatively natural compared to IVF-ET, and on the other hand, compared to the natural conception process, AIH bypasses many factors that may affect the ability to conceive, such as ovulation and sperm selection[18]. Our study was to assess the effect of COVID-19 inactivated vaccine doses on female reproduction using the AIH cycle as a model and using unvaccinated cycles as the reference. In grouping, rather than simply dividing men into vaccinated and unvaccinated groups, we paid close attention to vaccination doses and chose a more rigorous grouping method. In addition, we also followed up the data of male vaccination status while focusing on female vaccination status.

The study also had some limitations. First, the sample size was small, and about 90% of couples have an interval of 3 months or more between the last dose and insemination, an in-depth stratified analysis of the interval between vaccination and AIH was not possible. Second, statistical bias exists in retrospective studies. Although factors related to AIH success were included in multivariate logistic regression to correct for confounding, and GEE model was used to control for bias caused by multiple cycles of the same couple, it was impossible to identify and control for all confounding variables. Third, the study included infertile couples who received AIH treatment and did not represent couples who conceived naturally.

CONCLUSIONS

In this study, the investigation into the impact of different doses of the COVID-19 inactivated vaccine on female fertility within assisted insemination with husband's sperm (AIH) cycles did not reveal any significant differences in reproductive outcomes among the unvaccinated group, the 1 or 2 doses group, and the 3 doses group. The rates of biochemical pregnancy, clinical pregnancy, ongoing pregnancy, and live birth were comparable across the three groups, suggesting that the doses of the COVID-19 inactivated vaccine did not independently influence the reproductive outcomes of AIH cycles.

DECLARATIONS

Funding

This work was supported by Scientific Research Project of Shanxi Provincial Health Commission (No. 2023064).

Author contribution

YS designed the study, carried out data analysis, and drafted the manuscript. LZ, YJ and JW collected all relevant data. AZ conceived the study, participated in its design and coordination, and helped draft the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

All authors declare that the research was conducted in theabsence of any commercial or financial relationships that could be construed asa potential conflict of interest.

Data availability

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics approval

This study involving human participants were reviewed and approved by Ethics Committee of Yuncheng Central Hospital affiliated to Shanxi Medical University (No. YXLL2023009).

Disclosure Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Attestation Statement

Data in the study has not been previously published unless specified.

Data will be made available to the editors of the journal for review or query upon request.

REFERENCES

1. Xu Z, Wu Y, Lin Y, et al. Effect of inactivated COVID-19 vaccination on intrauterine insemination cycle success: A retrospective cohort study. Front Public Health 2022;10:966826.
2. Chen H, Zhang X, Lin G, et al. Safety of COVID-19 vaccination in women undergoing IVF/ICSI treatment - Clinical study and systematic review. Front Immunol 2023;13:1054273.
3. Gao Q, Bao L, Mao H, et al. Development of an inactivated vaccine candidate for SARS-CoV-2. Science 2020;369:77-81.
4. Wu Z, Hu Y, Xu M, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis 2021;21:803-812.
5. Xia S, Duan K, Zhang Y, et al. Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity Outcomes: Interim Analysis of 2 Randomized Clinical Trials. JAMA 2020;324:951-960.
6. Xia S, Zhang Y, Wang Y, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial. Lancet Infect Dis 2021;21:39-51.
7. Ayeleke RO, Asseler JD, Cohlen BJ, et al. Intra-uterine insemination for unexplained subfertility. Cochrane Database Syst Rev 2020;3:Cd001838.
8. Veltman-Verhulst SM, Hughes E, Ayeleke RO, et al. Intra-uterine insemination for unexplained subfertility. Cochrane Database Syst Rev 2016;2:Cd001838.
9. Wang C, Tang D, Liu J, et al. Association Between COVID-19 Vaccination and Artificial Insemination Outcomes for Couples Experiencing Infertility. JAMA Netw Open 2022;5:e2247216.
10. Nagy A, Alhatlani B. An overview of current COVID-19 vaccine platforms. Comput Struct Biotechnol J 2021;19:2508-2517.
11. Braun AS, Feil K, Reiser E, et al. Corona and Reproduction, or Why the Corona Vaccination Does Not Result in Infertility. Geburtshilfe Frauenheilkd 2022;82:490-500.
12. Dong M, Wu S, Zhang X, et al. Effects of COVID-19 vaccination status, vaccine type, and vaccination interval on IVF pregnancy outcomes in infertile couples. J Assist Reprod Genet 2022;39:1849-1859.
13. Shi W, Wang M, Xue X, et al. Association Between Time Interval from COVID-19 Vaccination to In Vitro Fertilization and Pregnancy Rate After Fresh Embryo Transfer. JAMA Netw Open 2022;5:e2236609.
14. Elhabak DM, Abdelsamie RA, Shams GM. COVID-19 vaccination and male fertility issues: Myth busted. Is taking COVID-19 vaccine the best choice for sperm protection and male fertility from risky infection hazards? Andrologia 2022;54:e14574.

15. Lestari SW, Restiansyah G, Yunihastuti E, et al. Comparison of sperm parameters and DNA fragmentation index between infertile men with infection and vaccines of COVID-19. Asian J Androl 2023;25:578-582.
16. Ma YC, Cheng C, Yuan C, et al. The effect of COVID-19 vaccines on sperm parameters: a systematic review and meta-analysis. Asian J Androl 2023;25:468-473.
17. Xia W, Zhao J, Hu Y, et al. Investigate the effect of COVID-19 inactivated vaccine on sperm parameters and embryo quality in in vitro fertilization. Andrologia 2022;54:e14483.
18. Leung ETY, Lee CL, Tian X, et al. Simulating nature in sperm selection for assisted reproduction. Nat Rev Urol 2022;19:16-36.