The Influence of COVID-19 on Human Fertility

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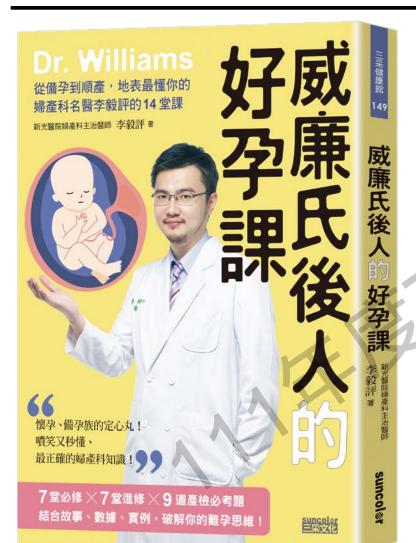
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威廉氏後人的好孕課:好評熱賣中!



全站暢銷榜

1. 靈覺醒 4 活出生命質感的高振動...

2. 【限量!排寒護持真言印記×語...

3. 尋寶記51: 曼谷尋寶記

4. 科學實驗王50: 宇宙大爆炸(隨...

5. 威廉氏後人的好孕課:從備孕到...

6. 撓場的科學:解開特斯拉未解之...

榮獲:北市醫師公會 第六屆『好書獎』肯定!



台北市醫師公會第六屆好書獎





Outline

- Introduction
- Effects of COVID-19 on Human Fertility
- Effects of COVID-19 on ART Outcomes
- Impact of COVID Vaccine on Human Fertility
- Take Home Message





Introduction





COVID-19 Pandemic

COVID-19 CORONAVIRUS PANDEMIC

Cases Timeline (worldwide)

Last updated: July 24, 2022, 01:26 GMT

Weekly Trends - Graphs - Countries - News

Coronavirus Cases:

574,547,238

view by country

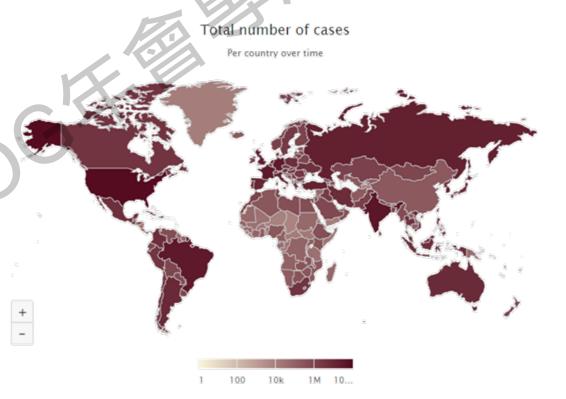
Deaths:

6,402,368

Recovered:

544,209,753





COVID-19 in Taiwan



各位防疫英雄,大家辛苦了!







散熱的方法只剩下傳導...







Approximately

1 in 5 adults

ages 18+ have a health condition that might be related to their previous COVID-19 illness, such as: Neurologic and mental health conditions*

Kidney failure

Musculoskeletal conditions

Cardiovascular conditions

Respiratory conditions

Blood clots and vascular issues



bit.ly/MMWR7121

Adults aged 65 and older at increased risk









台灣生殖醫學會會訊

國內郵資已付北區局營收股許可證北台字第12926號

印刷品

그는 아마 다니

2022年3月 發行日2022年5月

President's Note

COVID-19 與 mRNA 疫苗對於妊娠及生殖的影響

新光吳火獅紀念醫院生殖內分泌科 李維鈞醫師 / 李毅評主任

2019年,由嚴重急性呼吸道症候群冠狀病毒 2型 (SARS-CoV-2)造成的嚴重特殊傳染性肺炎 (Coronavirus disease 2019,COVID-19),迅速引發了一場規模空前的全球健康危機。由於其嚴重影響,多種 COVID-19 疫苗迅速開發、批准和生產。本文針對 COVID-19 對生殖系統的影響、COVID-19 是否會對孕婦造成垂直感染、mRNA 疫苗對於生殖系統的影響與mRNA 疫苗對於孕婦與胎兒的影響做了文獻回顧。





試管嬰兒補助案:110/7/1起



未滿45歲不孕夫妻

每胎6次(上限)

未滿 45歲 3次

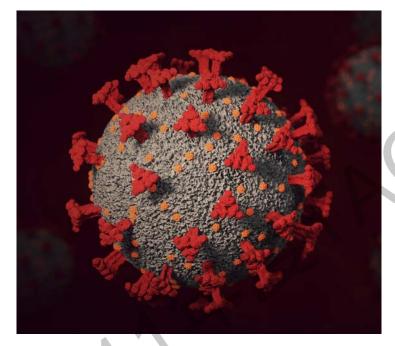
首次申請上限 10萬元 再次申請上限 6萬元

每年2萬3千~2萬8千對





當與病毒共存遇上試管嬰兒補助









COVID-19
Vaccine



SKH IVF Center COVID-19 Testing

Day 2 居家 快篩 快篩 (+)



建議先治療



下週期 再*入*療程

快篩(-)



做好個人 防護



取卵前 醫院快篩

確診者

確診 大於14天

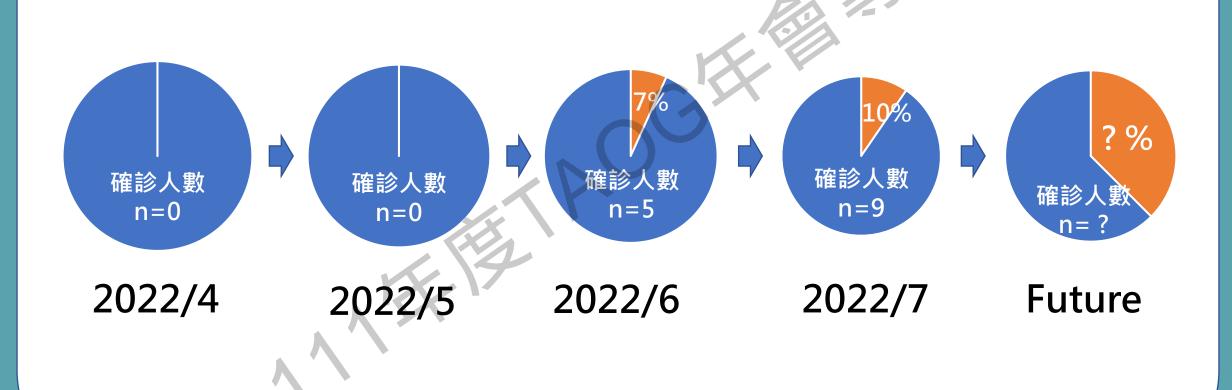


取卵前 不需採檢





SKH IVF Center Experience



Dr. Williams



COVID-19 & Human Fertility



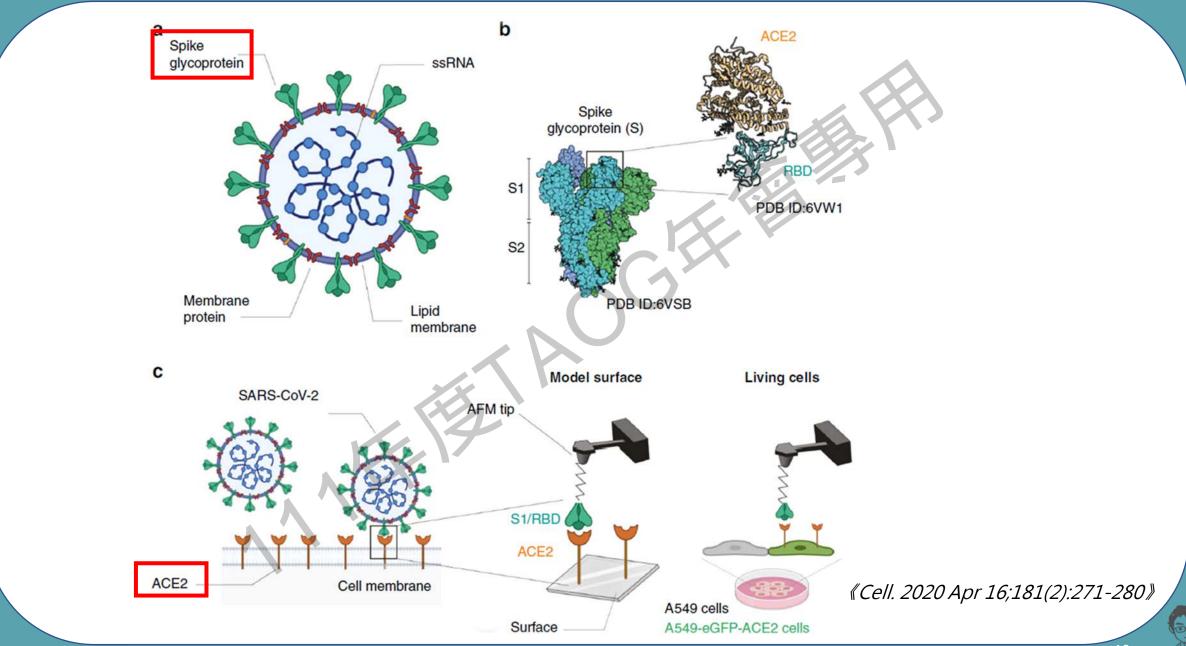


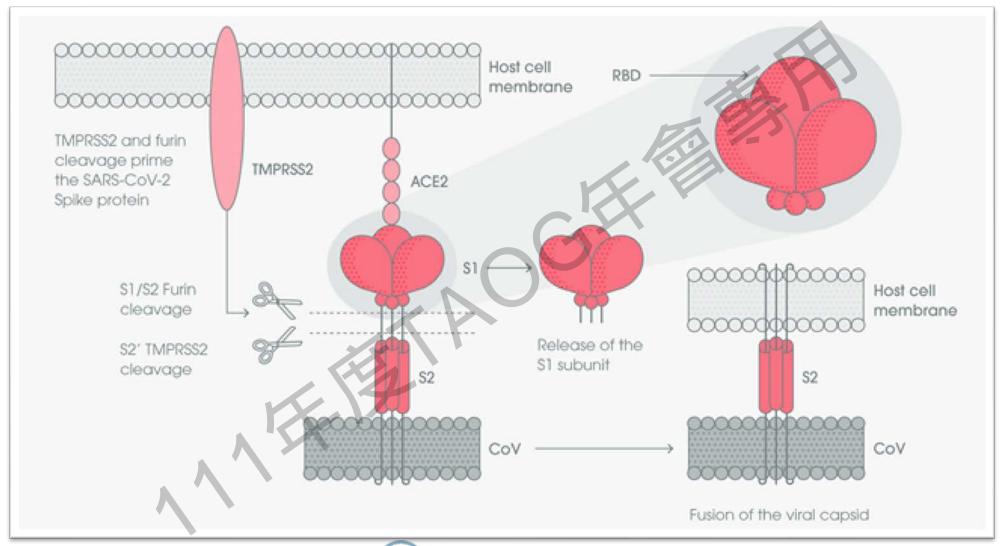
The Cell Entry Of SARS-CoV-2

- <u>Cell entry of coronaviruses</u> depends on binding of the spike (S) proteins to cellular receptors and S protein priming needs host cell proteases.
- SARS-CoV-2 uses the SARS-CoV receptor <u>ACE2</u> for entry and the serine protease <u>TMPRSS2</u> for assistance of cell entry.
- A TMPRSS2 inhibitor approved for clinical use blocked entry and might constitute a treatment option.

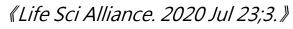














Advance Access Publication on February 1, 2021 doi:10.1093/humrep/deab026

human reproduction

ORIGINAL ARTICLE Infertility

Semen impairment and occurrence of SARS-CoV-2 virus in semen after recovery from COVID-19

M. Gacci^{1,*}, M. Coppi^{2,3}, E. Baldi^{2,4}, A. Sebastianelli¹, C. Zaccaro¹, S. Morselli¹, A. Pecoraro¹, A. Manera¹, R. Nicoletti¹, A. Liaci¹, C. Bisegna¹, L. Gemma¹, S. Giancane¹, S. Pollini^{2,3}, A. Antonelli^{2,3}, F. Lagi^{2,5}, S. Marchiani⁴, S. Dabizzi⁴, S. Degl'Innocenti F. Annunziato², M. Maggi⁶, L. Vignozzi⁴, A. Bartoloni^{2,5}, G.M. Rossolini^{2,3}, and S. Serni^{1,2}

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Table I SARS-CoV-2 positive rate in semen or testicular tissue and clinical characteristics among patients with COVID-19.

Study design	Sample		Infection stage			1	Reco	covery stage		Reproductive	Reference
		Positive	rate	Time from a tive swab to disease ons sample colle	est or et to	Positive r	ate	Time from c recovery to s collection	sample	system symptom	
Cohort study	Semen	26.7% (4	4/15)	4 patients with tive test results 6–I I days Others: not pro	range	8.7% (2/2	23)	2 patients with tive test results 3 days, respect Others: not pro	2 and evely	=	Li et al., 2020
Pilot cohort study	Semen	0 (0/	(2)	Not provided	P	0 (0/18)	Range 8–54 day	ys	Impaired sperm quality (4/18), testicular dis- comfort (1/18)	Holtmann et al., 2020
Cohort study	Semen	0 (0/		All the 23 subjection median 32 days		0 (0/11	5	All the 23 subje median 32 days		=	Guo et al., 2021
Cohort study	Semen	0 (0/		Range 0–7 days dian I day	, me-	-		=		=	Kayaaslan et al. 2020
Cohort study	Semen	0 (0/	12)	Range 5–109 d	ays	-		-		Low sperm motility (4/12)	Ma et al., 2021

《Hum Reprod. 2021 Dec 27;37(1):5-13.》



Table I SARS-CoV-2 positive rate in semen or testicular tissue and clinical characteristics among patients with COVID-19.

Study design	Sample	e Infec	tion stage	Reco	overy stage	Reproductive	Reference
		Positive rate	Time from a posi- tive swab test or disease onset to sample collection	Positive rate	Time from clinical recovery to sample collection	3711100111	
				可表			
Descriptive study	Semen	0 (0/1)	40 days	0 (0/11)	Range 14–42 days	_	Song et al., 2020
Observational, cross-sectional study	Semen		-	0 (0/34)	Not provided	Scrotal discomfort (6/ 34)	Pan et al., 2020
Prospective cross- sectional study	Semen			2.3% (1/43)	I patient with positive test results: 21 days Others: range 13– 67 days	Oligo-crypto-azoo- spermia (11/43)	Gacci et al., 2021
Case-controlled study	Semen		-	0 (0/70)	Range 64–93 days, median 80 days	Decreased sperm concentration	Ruan et al., 2021
Total	Semen	6.9% (4/58)) (1.4% (3/210)			



SARS-CoV-2 Positive Rate in Semen

- <u>Spermatogonia are the only cells coexpressing ACE2 and TMPRSS2 in</u> the testis.
- The positive rate of semen was only 1.4% in recovery stage, lower than 6.9% in patients in the acute stage.
- Time from disease onset to semen sample collection was mostly short (range 2-11 days) in patients with positive semen.



《Hum Reprod 2021;36:1520–1529.》



Journal of Assisted Reproduction and Genetics (2021) 38:1691–1708 https://doi.org/10.1007/s10815-021-02097-1

COMMENTARY



The probable destructive mechanisms behind COVID-19 on male reproduction system and fertility

Mojgan Moshrefi^{1,2,3} • Saeed Ghasemi-Esmailabad² • Jaffar Ali⁴ • Necati Findikli^{5,6} • Esmat Mangoli^{1,2} • Mohammad Ali Khalili^{1,2} •

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《J Assist Reprod Genet . 2021 Jul;38(7).》



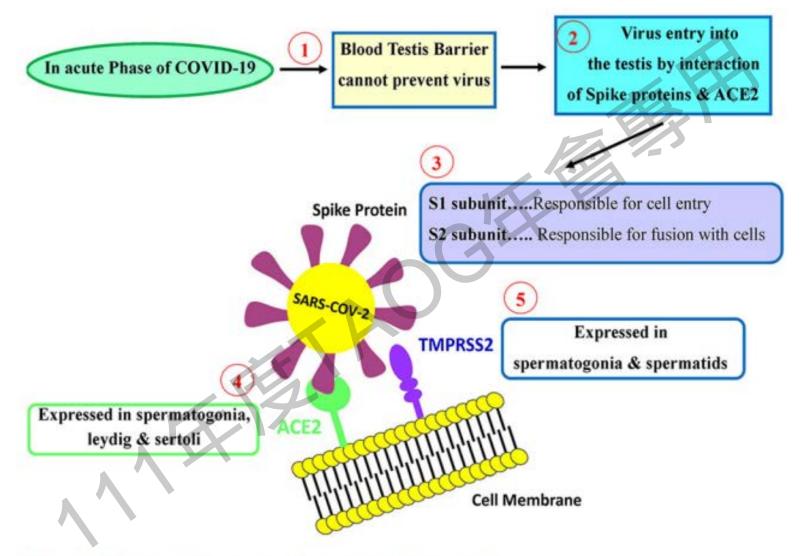


Fig. 1 The mechanisms of virus entry to cells

《J Assist Reprod Genet . 2021 Jul;38(7).》



Inflammation Research

ORIGINAL RESEARCH PAPER



COVID-19 disrupts the blood-testis barrier through the induction of inflammatory cytokines and disruption of junctional proteins

Tahmineh Peirouvi¹ · Abbas Aliaghaei² · Bahram Eslami Farsani³ · Sanaz Ziaeipour² · Vahid Ebrahimi⁴ · Mehdi Forozesh⁵ · Masoud Ghadipasha⁵ · Gholam-Reza Mahmoudiasl⁶ · Arefeh Aryan⁷ · Negin Moghimi^{1,2} · Shabnam Abdi⁸ · Amir Raoofi⁹ · Mohammadhossein Kargar Godaneh² · Mohammad-Amin Abdollahifar²

Received: 3 June 2021 / Revised: 18 August 2021 / Accepted: 20 August 2021 / Published online: 26 August 2021 © The Author(s), under exclusive licence to Springer Nature Switzerland AG 2021



《 Inflamm Res . 2021 Dec;70(10-12)》



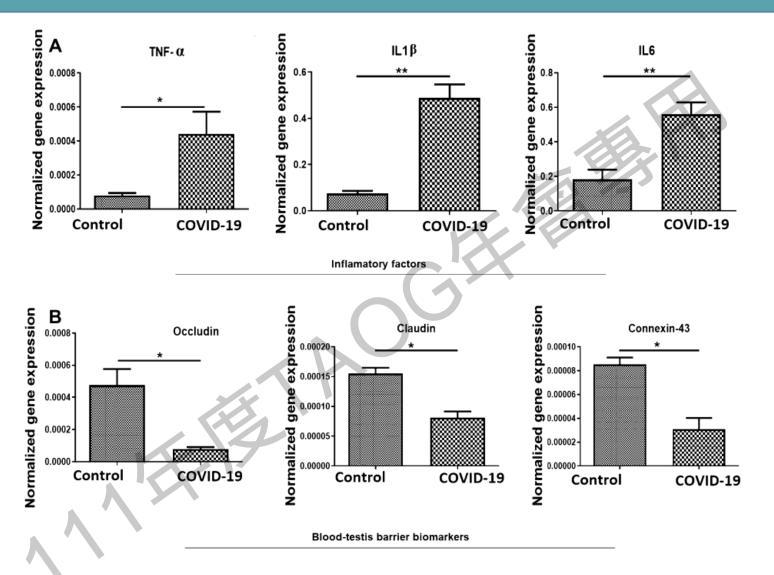


Fig. 2 The effect of SARS-CoV-2 on the inflammatory cytokines and junctional proteins in the human post-mortem testicular tissue. A and B Real-time PCR analyses of testes. mRNA expression levels of TNF- α , IL1 β , IL6, claudin-11, occludin and connexin-43 from

control and COVID-19 groups. Mean \pm SD of the mRNA expression levels of TNF- α , IL1 β , IL6, claudin-11, occludin and connexin-43 of testis in the study groups (*p<0.05 and **p<0.01)

《 Inflamm Res . 2021 Dec;70(10-12)》



Infection or Contamination?

- The probability of <u>viral contamination</u> from non-semen sources could not be completely ruled out.
- Most semen samples were collected by masturbation, and <u>the virus on</u>
 <u>the epidermis</u> was likely to cause contamination.
- <u>Aerosols</u> are the main transmission routes of SARS-CoV-2, and most semen was not using aerosol-tight caps during sample collection.

《Hum Reprod. 2021 Dec 27;37(1):5-13.》





Masturbation Without Contamination?



安捏是安怎取精???





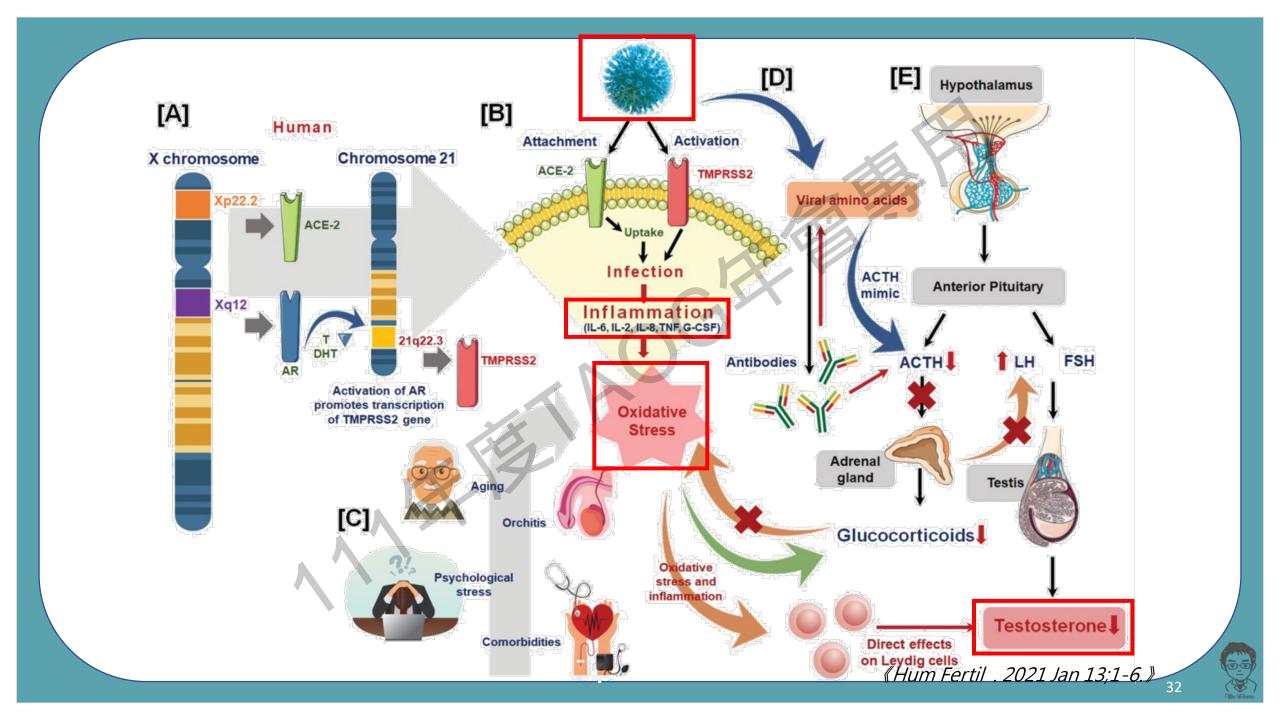
COVID-19 and Hypogonadism:

- However low sperm motility (33.3%) and oligospermia (25.5%) were found in COVID-19 infected men even in recovery stage.
- Low testosterone levels were also found in male patients.

《Hum Fertil . 2021 Jan 13;1-6.》







Brief Summary: COVID-19 & Male

- SARS-CoV-2 could disrupt blood-testis barrier via TNF- α , IL1 β , IL6.
- However, shedding of SARS-CoV-2 into the semen is rare.
- <u>Hypoxia and oxidative stress</u> may contribute to decreased semen parameters.
- The probability of <u>viral contamination</u> could not be ruled out.
- Whether SARS-CoV-2 can infect the male reproductive system remains controversial.

 On Dr. Williams

 (Hum Reprod. 2021 Dec 27;37(1):5-13.)

PLOS ONE



Female reproductive tract has low concentration of SARS-CoV2 receptors

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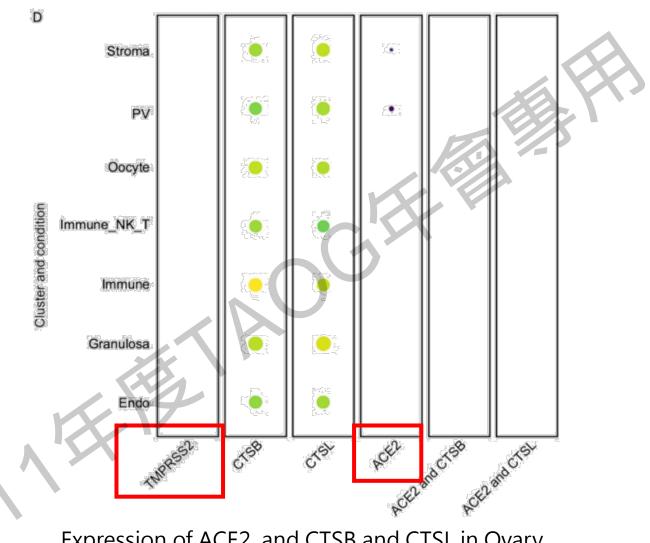
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《PLoS One. 2020 Dec 14;15(12)》



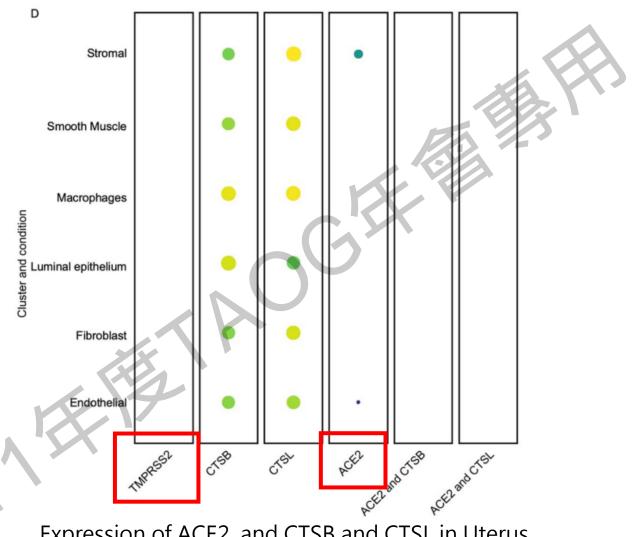


Expression of ACE2, and CTSB and CTSL in Ovary



《PLoS One. 2020 Dec 14;15(12)》





Expression of ACE2, and CTSB and CTSL in Uterus



《PLoS One. 2020 Dec 14;15(12)》



Female Reproductive Organs Are Unlikely to Be Infected by SARS-CoV2.

- None of the cell types in the female reproductive organs showed the co-expression of ACE2 with proteases TMPRSS2, known to facilitate the entry of SARS2-CoV2 into the host cell.
- These results suggest that uterus and ovaries <u>are unlikely to be</u> <u>susceptible to SARS-CoV2 infection</u>.
- However, the overall effects of COVID-19 on the female reproductive system have remained unclear.





RBMO





ARTICLE



Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age



BIOGRAPHY

Dr Kezhen Li is a gynaecologist at the Department of Gynecology and Obstetrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China. Her research interests include ovarian endocrinology and oncofertility.

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TABLE 1 CLINICAL CHARACTERISTICS OF FEMALES WITH COVID-19

	Mild (n = 147)	Severe (n = 90)	P-value
Age, years, median (IQR)	36.00 (31.00–41.00)	37.00 (32.75–41.00)	0.13
Death rate	0 (0)	3 (3)	0.05
Complications			
Abnormal hepatic function	5 (3)	6 (7)	0.34
Abnormal renal function	4 (3)	4 (4)	0.48
Cardiac function injury	14 (10)	16 (18)	0.06
Digestive system injury	29 (20)	23 (26)	0.29
Respiratory system injury	96 (65)	66 (73)	0.20
Nervous system injury	0 (0)	8 (9)	< 0.001
Treatments			
Antiviral therapy	132 (90)	74 (82)	0.09
Antibiotics	99 (67)	56 (62)	0.42
Glucocorticoid therapy	38 (26)	26 (29)	0.61
Intravenous immunoglobulin the	erapy 19 (13)	20 (22)	0.06
Oxygen treatment			
High flow nasal cannula	96 (65)	59 (66)	0.97
Mechanical ventilation	0 (0)	7 (7)	0.001



SPO2≤95% at rest,

Respiratory distress,

PaO₂/FiO₂ ≤300 mmHg,

Mechanical ventilation,

Shock,

ICU admission



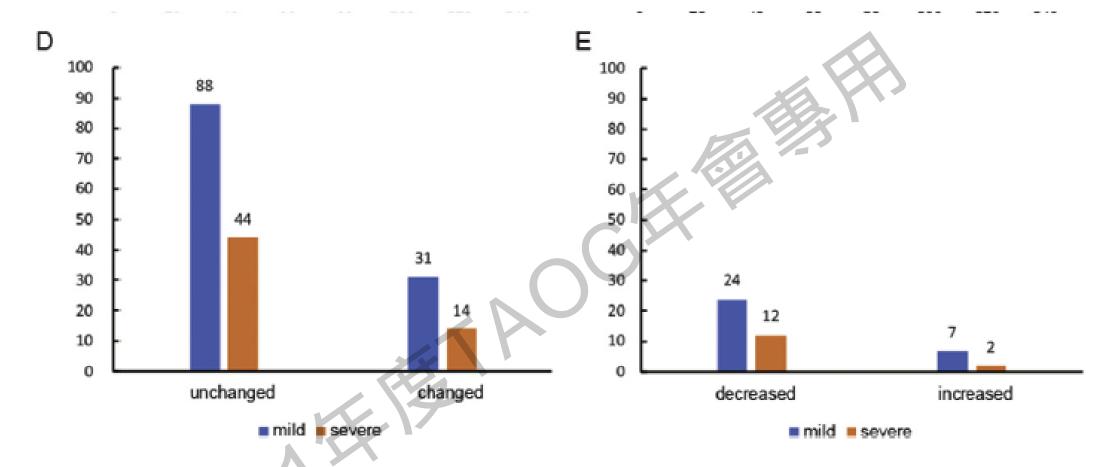


FIGURE 1 Menstrual volume changes of women with COVID-19. (A) Overall menstrual volume changes. (B) Menstrual volume changes of mildly ill patients. (C) Menstrual volume changes of severely ill patients. (D) Comparison of total menstrual volume changes in mild and severe patients (chi-squared test, P = 0.784). (E) Comparison of increased and decreased menstrual volume in mild and severe patients (chi-squared test, P = 0.698).





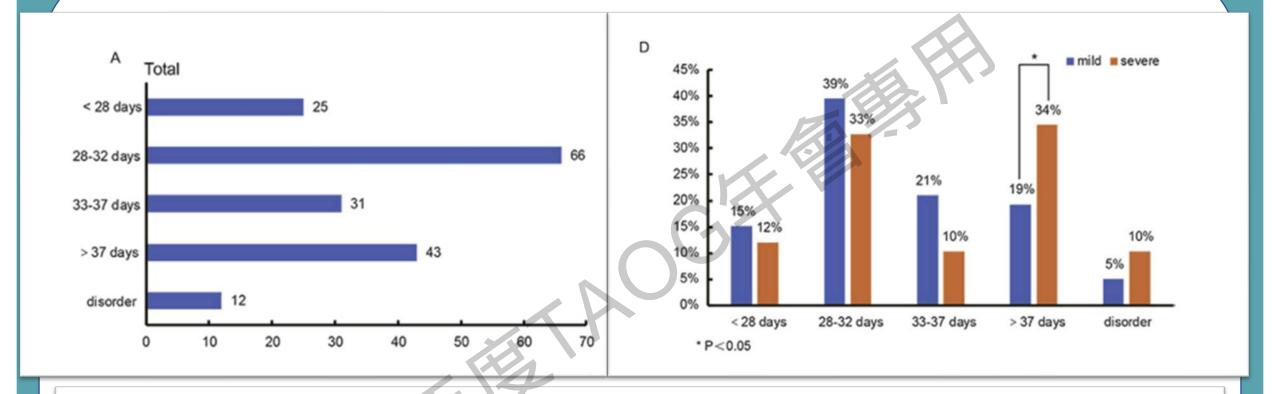


FIGURE 2 Menstrual cycle of women with COVID-19. (A) Overall menstrual cycle distribution. (B) Menstrual cycle distribution of mildly ill patients. (C) Menstrual cycle distribution of severely ill patients. (D) Comparison of menstrual cycles in mildly and severely ill patients. <28 days P = 0.584, 28–32 days P = 0.384, 33–37 days P = 0.08, >37 days P = 0.001, disordered P = 0.211.





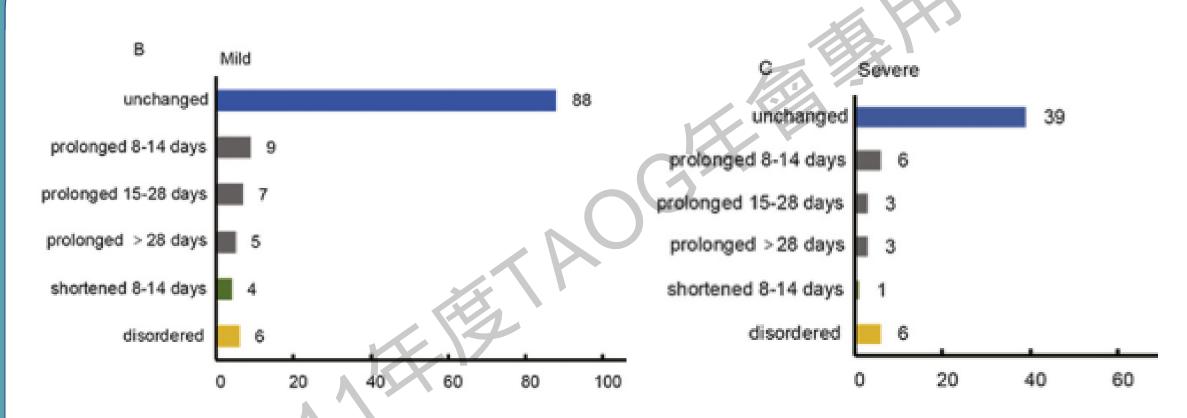


FIGURE 3 Menstrual cycle changes of women with COVID-19. (A) Overall menstrual cycle changes. (B) Menstrual cycle changes of mildly ill patients. (C) Menstrual cycle changes of severely ill patients. (D) Comparison of menstrual cycle changes in mildly ill and severely ill patients. (E)





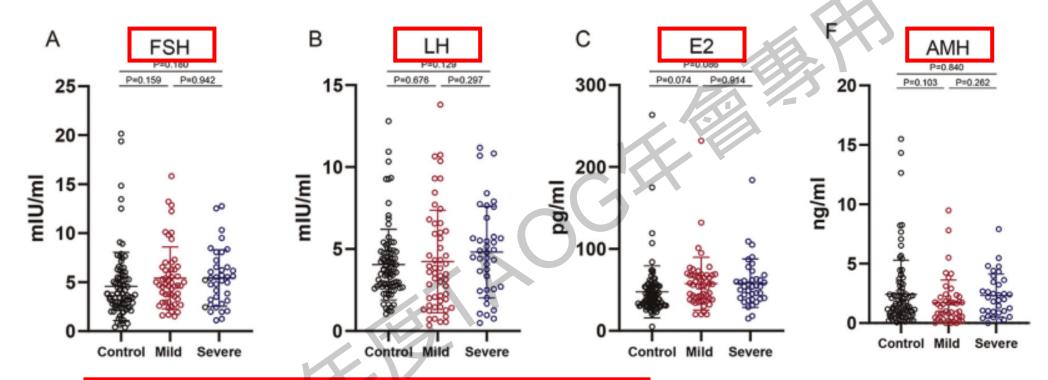


FIGURE 4 Sex hormone and AMH concentrations of mild and severe COVID-19 patients compared with the controls. (A) FSH of mildly and severely ill COVID-19 patients compared with control. (B) LH of mildly and severely ill COVID-19 patients compared with the control. (C) E2 of mildly and severely ill COVID-19 patients compared with the control. (E) T of mildly and severely ill COVID-19 patients compared with the control. (F) AMH of mildly and severely ill COVID-19 patients compared with the control. Data are shown as the mean ± SD. AMH = anti-Müllerian hormone; E2 = oestradiol; P = progesterone; T = testosterone.

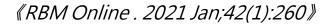




COVID-19 & Menstruation

- 25% COVID-19 patients presented with menstrual volume changes, and 28% patients had menstrual cycle changes, mainly a <u>decreased</u> volume (20%) and a <u>prolonged cycle</u> (19%).
- The average <u>sex hormone</u> and <u>AMH</u> concentrations of women of childbearing age with COVID-19 were <u>not changed</u>.
- The menstruation changes might be the consequence of <u>transient</u> <u>suppression of ovarian function</u> that quickly resume after recovery.







COVID-19 & ART Outcomes





Human Reproduction, Vol.37, No.5, pp. 947-953, 2022

Advance Access Publication on February 25, 2022 https://doi.org/10.1093/humrep/deac043

human reproduction

ORIGINAL ARTICLE Infertility

IVF under COVID-19: treatment outcomes of fresh ART cycles

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Submitted on December 12, 2021; resubmitted on February 16, 2022; editorial decision on February 21, 2022



Group	COVID-19 (N = 121)	Non-COVID-19 (N = 121)	P-value
Patient age (year)	33.3 (5.37) [21–42]	33.23 (5.33) [22–42]	0.896
Partners age (year)	35.78 (6.90) [22–55]	34.39 (5.45) [21–48]	0.2
Smoker	14 (12%)	17 (15%)	0.445
Previous retrievals	1.07 (1.60) [0-8]	1.19 (1.48) [0.00–8.00]	0.156
Previous transfers	1.11 (2.18) [0-12]	1.25 (1.92)	0.087
вмі	25.25 (5.55) [16.23-42.97]	25.48 (5.86) [16.53-42.45]	0.959
Infertility cause (N)	110	102	0.209
Age related	14 (13%)	19 (19%)	
Male factor	32 (29%)	35 (34%)	
Ovulation	6 (5%)	11 (11%)	
Mechanical	11 (10%)	4 (4%)	
Unexplained	27 (25%)	17 (16%)	
Fertility preservation	12 (11%)	8 (8%)	
Other	8 (7%)	8 (8%)	
Parity (N)	104	95	0.519
0	71 (68%)	66 (70%)	
1	19 (18%)	21 (22%)	
≥2	14 (14%)	8 (8%)	
Days from COVID to oocyte	84.54 (78.02) [8–348]	NA	
retrieval			
≤90	77 (64%)	NA	
>90–180	29 (24%)	NA	
>180	15 (12%)	NA	

Table III. Cycle characteristics and outcomes of COVID versus control group—fresh embryo transfer cycle.

Group	COVID-19 (N = 91)	Non-COVID-19 (N = 94)	P-value
Gonadotropin dosage (IU)	2529.42 (1418) [600 — 7800]	2334.70 (1269) [600 – 6600]	0.365
Max. E2 (pmol/l)	7598 (5375) [1337 — 28 382]	7510 (5151) [456 – 25 022]	0.939
Endometrial thickness (mm)	10.75 (2.25) [6 – 17]	9.99 (2.22) [5.4 – 15]	0.062
Oocytes retrieved	II.26 (6.19) [I — 33]	10.04 (6.90) [1 – 31]	0.085
Fertilization method	91	93	0.009
ICSI	64 (70%)	46 (50%)	
ICSI/IVF	22 (24%)	33 (35%)	
IVF	5 (6%)	14 (15%)	
Percent MII/oocytes (ICSI) (N)	64	46	0.072
	77.60 (18.87) [25 — 100]	83.08 (19.98) [33 – 100]	
Fertilization rate	0.59 (0.24) [0.07 – 1]	0.62 (0.26) [0 - 1]	0.365
Total frozen embryos	1.71 (2.40) [0 – 15]	2.12 (2.34) [0 - 11]	0.168
Clinical pregnancy	39 (43%)	38 (40%)	0.737
Partner COVID status (N)	63	68	< 0.001
Recovered	40 (63%)	0	
Vaccinated	13 (21%)	7 (10%)	
Non	10 (16%)	61 (90%)	



IVF Under COVID-19

- One 121 infected patients and 121 controls who underwent fresh ART cycles were included.
- Oocyte yield (12.50 versus 11.29; P = 0.169), mature oocyte rate (78% versus 82%; P = 0.144), fertilization rates, number of frozen embryos per cycle and clinical pregnancy rates (43% versus 40%; P = 0.737) in all fresh cycles were similar between groups.

《Hum Reprod . 2022 May 3;37》





COVID Vaccine & Human Fertility





Research Letter

FREE

June 17, 2021

Sperm Parameters Before and After COVID-19 mRNA Vaccination

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» Author Affiliations | Article Information

JAMA. 2021;326(3):273-274. doi:10.1001/jama.2021.9976







Sperm Parameters & COVID-19 Vaccination

- 45 volunteer (median age, 28 years [25-31]); follow-up samples were obtained at a median of 75 days [70-86] after the 2nd dose of vaccine.
- Of the 45 men, 21 (46.7%) received <u>Pfizer-BioNTech</u> and 24 (53.3%) received <u>Moderna</u>, baseline median sperm concentration and TMSC were 26 million/mL and 36 million, respectively.
- After the 2^{nd} dose, the median sperm concentration and the median TMSC increased to 30 million/mL (P = 0.02) and to 44 million (P = 0.001), respectively.

Dr. Williams



Change in Semen Analysis Parameters Before and After COVID-19 Vaccination

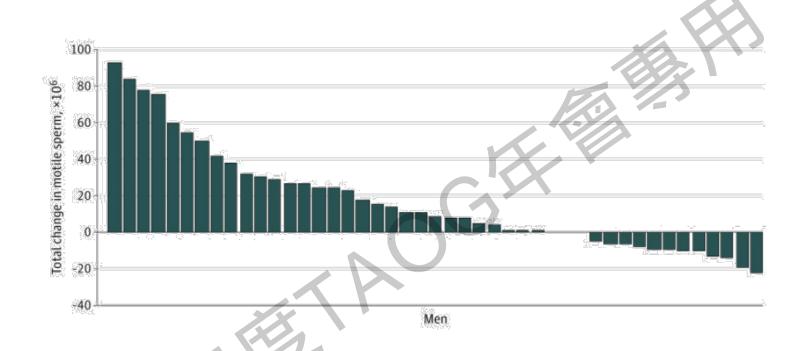
Parameter	Normal value	e Median (IQF	0	P value
		Baseline	Follow-up	
No. of participants		45	45	
Volume, mL	>1.5	2.2 (1.5-2.8)	2.7 (1.8-3.6)	.01
Sperm concentration, mill	ion/mL >15	26 (19.5-34)	30 (21.5-40.5)	.02
Total motility, %	>40	58 (52.5-65)	65 (58-70)	.001
TMSC, million	>9	36 (18-51)	44 (27.5-98)	.001

Abbreviations: IQR, interquartile range; TMSC, total motile sperm count.





Figure.



Waterfall Plot Showing Changes in Total Motile Sperm Count Parameters Within Participants Before and After COVID-19 Vaccination

Each bar represents an individual participant.





Advance Access Publication on August 7, 2021 doi:10.1093/humrep/deab182

human reproduction ORIGINAL ARTICLE Reproductive biology

Ovarian follicular function is not altered by SARS-CoV-2 infection or BNT162b2 mRNA COVID-19 vaccination

- Y. Bentov (1,2,3,*,†, O. Beharier^{1,2,3,†}, A. Moav-Zafrir^{1,2,3}, M. Kabessa^{1,2,3}, M. Godin^{1,2,3}, C.S. Greenfield^{1,2,3},
- M. Ketzinel-Gilad^{1,2,3}, E. Ash Broder^{1,2,3}, H.E.G. Holzer^{2,3}, D. Wolf^{3,4}, E. Oiknine-Djian^{3,4}, I. Barghouti^{3,5}, D. Goldman-Wohl^{1,2,3}, S. Yagel^{1,2,3}, A. Walfisch^{1,2,3}, and A. Hersko Klement^{1,2,3}

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Table I Demographics of patients in a study of the effects of immune response to COVID-2019 or an mRNA vaccine on the ovarian follicle.

		Vaccine	COVID	Control**	Total	
Number		9	9		32	P-value
Age (years)	Mean \pm (SD) Median	35.3 ± 3.97 35	34.1 ± 4.7 34	32.5 ± 5.3 33	33.75 (± 4.8) 34	0.383
AFC	Mean (SD) Median	13.3 ± 4.7 14	13.6 ± 4.1	15.6 ± 6.7 17.5	14.4 ± 5.7 14.5	0.592
Indication	Male (%) Non male (%) Egg freeze (%) Non-infertile	2 (22.2%) 2 (22.2%) 5 (55.6%) 7 (77.8%)	1 (11.1%) 5 (55.6%) 3 (33.3%) 4 (44.4%)	4 (28.6%) 9 (64.3%) 1 (7.1%) 5 (35.7%)	7 (21.9%) 16 (50%) 9 (28.1%) 16 (50%)	0.113
Time interval *	Mean SD	32.2 22.1	98.14 45.5	N/A N/A		0.003

Univariate ANOVA was used for analysis of age, AFC and time interval and Chi-square for analysis of indication.

COVID-19, coronavirus disease 2019; AFC, antral follicle count.



《Hum Reprod . 2021 Aug 18;36.》



^{*}Time interval (days) from recovery or first vaccine to the day of oocyte retrieval.

^{**}Non-vaccinated-non infected patients.

Table III IVF treatment outcome parameters.

Parameter	Group Number	Vaccine 9	COVID 9	Control 14	Total 32	P-value
Trigger day estradiol (pmol/l)	Mean (SD) Median	8874 ± 2555 8507	10 810 ± 5867 9913	6354±2657 6155	8379 ± 4167 8506	0.351
Trigger day progesterone (nmol/l)	Mean (SD) Median	3.29 ± 2.09 2.63	3.31 ± 1.14 3.26	1.64±0.67	2.6 ± 1.54 2.46	0.008
Type of trigger	hCG only (%) GnRHa (%) Dual (%)	I (II.1%) 4 (44.4%) 4 (44.4%)	0 4 (44.4%) 5 (55.6%)	1 (7.1%) 4 (28.6%) 9 (64.3%)	2 (6.3%) 12 (37.5%) 18 (56.3%)	0.766
Oocyte retrieval serum estradiol (pmol/ml)	Mean (SD) Median	4133 ± 1212 3880	5321 ± 1884 4982	3535 ± 1855 3070	4206 ± 1891 3995	0.082
Oocyte retrieval serum progesterone (nmol/l)	Mean (SD) Median	22.6 ± 16.4 15.8	26.5 ± 12.1 23.5	18.6 ± 10.5 13.5	22 ± 13.5 17.85	0.40
Number of oocytes	Mean (SD) Median	12.4 ± 8.7 8	10.89 ± 4.8 10	11.2 ± 6.7 10	11.5 ± 6.7 9	0.877
Number of mature oocytes	Mean (SD) Median	7.25 ± 2.77 6.5	8.37 ± 4.1 7	7.75 ± 4.7 6.5	7.8 ± 4.1 7	0.870
GQ Day 3/2PNs	Mean (SD) Median	0.43 ± 0.05 0.43	0.55 ± 0.14 0.48	0.72 ± 0.34 0.86	0.63 ± 0.3 0.5	0.314

Univariate ANOVA was used for analysis of all the parameters included in this table.

GnRHa, GnRH agonist; HSPG2, heparan sulfate proteoglycan 2; PN, pronuclei; GQ, good quality embryos.

《Hum Reprod . 2021 Aug 18;36.》

Infected or Vaccinated

- This is the first study to examine the impact of SARS—Cov-2 infection and vaccination on ovarian function and these early findings suggest no measurable detrimental effect on function of the ovarian follicle.
- Ovarian follicular function is not altered by SARS–CoV-2 infection or BNT162b2 mRNA COVID-19 vaccination.





Original Research

In Vitro Fertilization and Early Pregnancy Outcomes After Coronavirus Disease 2019 (COVID-19) Vaccination

Devora Aharon, MD, Matthew Lederman, MD, Atoosa Ghofranian, MD, Carlos Hernandez-Nieto, MD, Chelsea Canon, MD, William Hanley, BA, Dmitry Gounko, MA, Joseph A. Lee, BA, Daniel Stein, MD, Erkan Buyuk, MD, and Alan B. Copperman, MD

490 VOL. 139, NO. 4, APRIL 2022

OBSTETRICS & GYNECOLOGY



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Table 1. Baseline Demographics, Cycle Characteristics, and Cycle Outcomes Among Vaccinated and Unvaccinated Patients Undergoing Controlled Ovarian Hyperstimulation

Variable	Vaccinated (n=222)	Unvaccinated (n=983)	P
Age (y)	36.7±4.4	37.1±4.5	.19
BML (kg/m ²)	24.3±4.6	24.9±5.0	.30
AMH (ng/mL)	2.9±2.9	2.7±2.6	.38
AFC	14.9±10.1	13.9±8.5	.33
Gravidity	0.0 (0.0–7.0)	0.0 (0.0–8.0)	.30
Parity	0.0 (0.0–3.0)	0.0 (0.0–4.0)	.01
Stimulation protocol			.02
Antagonist	92.3	86.2	.01
Flare	6.3	12.8	.005
Down-regulation	1.4	1.0	.71
Cumulative gonadotropin dosage (international units)	3,954.0±1,392.5	$3,927.3\pm1,317.9$.78
Estradiol at trigger (pg/mL)	2,559.4±1,371.2	2,513.7±1,256.1	.91
Embryo biopsy for PGT-A	79.7	78.6	.72
Average biopsy day*			.28
5	59.9	54.2	
6	36.7	40.1	
7	3.4	5.7	
Fertilization rate (%)	80.7 [78.4–83.0]	78.7 [77.5–80.0]	.39
No. of eggs retrieved	15.9 [14.4–17.5]	15.0 [14.4–15.6]	.64
No. of mature oocytes retrieved	12.2 [11.0–13.3]	11.2 [10.7–11.7]	.20
Mature oocytes ratio (%)	77.2 [75.0–79.3]	74.7 [73.5–75.8]	.18
Blastulation rate (%)	62.9 [59.4–66.4]	60.0 [58.2–61.7]	.30
Euploid rate (%)*	48.8 [44.1–53.6]	42.5 [40.2–44.9]	.02



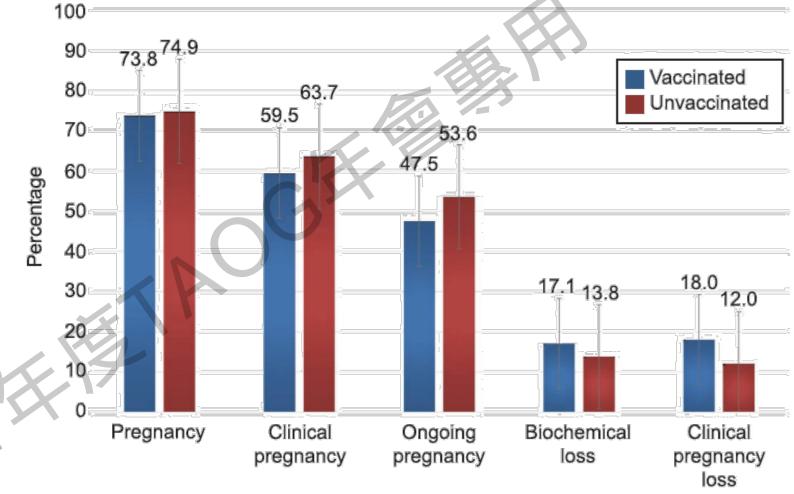


Fig. 2. Single euploid frozen-thawed embryo transfer outcomes between fully vaccinated and unvaccinated patients. *Error bars* represent 95% Cls.

Aharon. COVID-19 Vaccination and IVF Outcomes. Obstet Gynecol 2022.



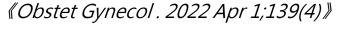
《Obstet Gynecol . 2022 Apr 1;139(4)》



COVID-19 Vaccination & IVF

- Patients fully vaccinated with a <u>COVID-19 mRNA vaccine</u> were compared with unvaccinated patients who cycled during the same time period.
- Administration of COVID-19 mRNA vaccines was <u>not associated with</u> an adverse effect on IVF outcomes.
- Our findings showed the safety of COVID-19 vaccination in women who are trying to receive IVF treatment.







https://doi.org/10.1093/humrep/deac160

human reproduction

ORIGINAL ARTICLE Infertility

Inactivated COVID-19 vaccination does not affect in vitro fertilization outcomes in women

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Yixuan Wu (1,2,3,4,†, Mingzhu Cao (1,2,3,4,†, Yanshan Lin<sup>1,2,3,4,†</sup>, Zijin Xu<sup>1,2,3,4</sup>, Zhu Liang<sup>1,2,3,4</sup>, Qing Huang<sup>1,2,3,4</sup>, Sichen Li<sup>1,2,3,4</sup>, Lei Li (1,2,3,4), Yaming Meng<sup>1,2,3,4</sup>, Chunyan An<sup>1,2,3,4</sup>, Haiying Liu (1,2,3,4,*, and Jianqiao Liu (1,2,3,4,*)
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Table II Baseline characteristics of the vaccinated versus the unvaccinated group.

	Vaccinated	Unvaccinated	P
n	240	1343	
Female age (year)	33.8 ± 4.7	33.4 ± 4.7	0.200
Male age (year)	35 (32, 40)	35 (31, 38)	0.119
Infertility duration (year)	4 (3, 6)	4 (2.5, 6)	0.967
AMH (ng/ml)	2.65 (1.28, 4.00)	2.52 (1.49, 4.12)	0.750
Total AFC	14.5 (10, 19)	16 (11, 21)	0.009
BMI (kg/m ²)	22.4 ± 3.0	22.4 ± 3.2	0.933
No. of previous OPU cycles	0 (0, 0)	0 (0, 1)	0.555
Causes of infertility % (n)			0.088
Male	20.0 (48)	18.8 (252)	
Tubal factors	48.8 (117)	49.1 (660)	
Ovulatory disorder	8.8 (21)	7.8 (105)	
Endometriosis	4.2 (10)	3.0 (40)	
Unexplained infertility	5.4 (13)	11.2 (151)	
Mixed factors	12.8 (31)	10.1 (135)	





	V accinated ^c	Unvaccinated ^c	P
n	239	928	
Oocytes retrieved	8 (5, 12)	9 (5, 12)	0.244
Fertilization rate % (n)	80.0 (1642/2053)	79.7 (6623/8314)	0.747
Fertilization type			0.412
IVF	70.3 (168)	74.5 (691)	
ICSI	26.8 (64)	23.3 (216)	
IVF + ICSI	2.9 (7)	2.3 (21)	
Blastulation rate ^a % (n)	48.9 (465/951)	49.3 (1937/3927)	0.812
No. of blastocytes	1 (0, 3)	I (0, 3)	0.229
No. of frozen embryos	1 (0, 3)	1 (0, 3)	0.255
No. of embryos suitable for transfer ^b	3 (2, 4)	3 (2, 4)	0.266
No. of embryos transferred			0.951
	56.9 (136)	56.7 (526)	
2	43.1 (103)	43.3 (402)	
Days of embryos transferred			0.439
3	79.1 (189)	76.7 (712)	
5	20.9 (50)	23.3 (216)	



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Rates % (n)	Vaccinated	Unvaccinated	Р
n	239	928	
Implantation	35.4 (121/342)	38.3 (509/1330)	0.325
Biochemical pregnancy	47.3 (113/239)	51.6 (479/928)	0.232
Clinical pregnancy	44.4 (106/239)	47.4 (440/928)	0.398
Biochemical pregnancy loss	6.2 (7/113)	9.6 (39/479)	0.487
Early miscarriage	15.0 (17/113)	12.1 (58/479)	0.399
Ectopic pregnancy	2.7 (3/113)	2.5 (12/479)	1.000 ^a
Ongoing pregnancy	36.0 (86/239)	39.9 (370/928)	0.272

^aFisher's exact test was used.





COVID Vaccination & IVF Outcomes

- This was a retrospective cohort study performed at 240 women vaccinated with either CoronaVac (科興) or Sinopharm (國藥) before ovarian stimulation.
- The rates of <u>ongoing pregnancy</u> (36.0% vs 39.9%, P=0.272), <u>implantation</u> (35.4% vs 38.3%, P=0.325), <u>biochemical pregnancy</u> (47.3% vs 51.6%, P=0.232), <u>clinical pregnancy</u> (44.4% vs 47.4%, P=0.398) and <u>early miscarriage</u> (15.0% vs 12.1%, P=0.399) were <u>not significantly different</u> between the vaccinated and the unvaccinated groups.



Take Home Message



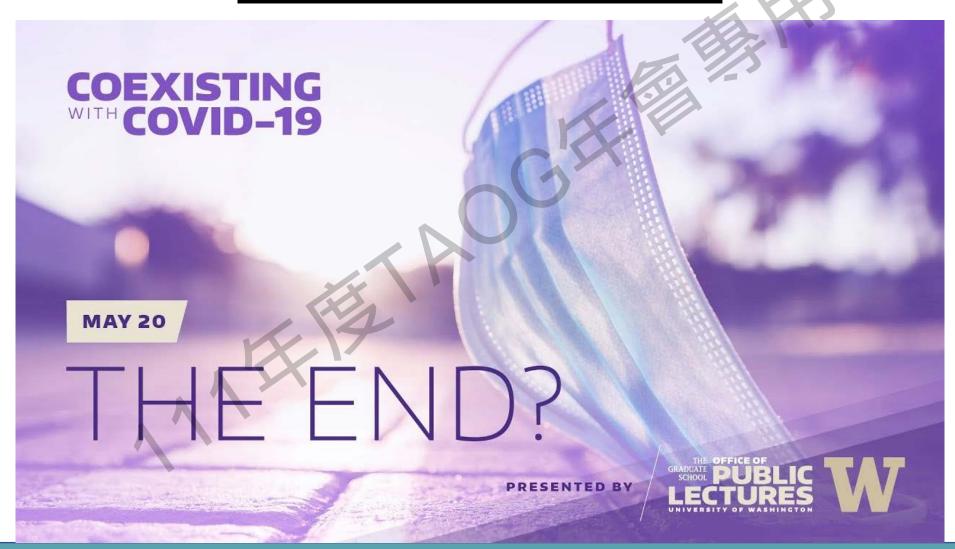


Take Home Message

- <u>Low sperm motility and oligospermia</u> were found in COVID-19 infected men, maybe due to hypoxia and oxidative stress.
- Without the co-expression of ACE2 and TMPRSS2, <u>female reproductive organs are</u> <u>unlikely</u> to be susceptible to SARS-CoV2 infection.
- COVID-19 patients presented with <u>decreased volume and a prolonged cycle</u>, and it might be the consequence of transient suppression of ovaries.
- Ovarian function and IVF outcomes seems to be not altered by SARS–CoV-2 infection or COVID-19 vaccination.



What's Next?





Thanks For Listening!



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