

# The Impact of Coronavirus Disease-2019 on Men with Primary Infertility: Case Report

© Ahmet Salvarci<sup>1</sup>, © Ali Sami Gurbuz<sup>2</sup>, © Fuat Ali<sup>3</sup>

<sup>1</sup>Novafertile and Medicana Hospital IVF Centers, Medicana Hospital Affiliated with KTO Medical Faculty, Department of Urology, Konya, Turkiye

<sup>2</sup>Novafertile and Medicana Hospital IVF Centers, Medicana Hospital Affiliated with KTO Medical Faculty, Department of Obstetrics and Gynecology, Konya, Turkiye

<sup>3</sup>Novafertile IVF Centers, Department of Obstetrics and Gynecology, Konya, Turkiye

## Abstract

At present, the world is faced with the coronavirus disease-2019 (COVID-19) threat caused by another novel coronavirus, the severe acute respiratory syndrome coronavirus 2. A 29-year-old patient diagnosed with primary infertility had COVID-19. Temporary severe oligo-astheno-teratozoospermia was observed in the long term; however, permanent losses occurred in rapid progressive sperms. His total testosterone level and total motile sperm count were permanently reduced. Permanent reductions occurred in his testicular volumes. But semen analysis values before COVID-19 was observed again. Pregnancy with intra cytoplasmic sperm injection was achieved with a high fertilization rate.

**Keywords:** COVID-19, infertility, pregnancy

## Introduction

Men are observed to be more affected by the highly contagious coronavirus disease-2019 (COVID-19) caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) compared to women (male/ratio rate is 2.7:1) (1). In addition, a negative impact occurs in spermatogenesis and testes (2). The virus is not necessarily directly present to cause harm to the male reproductive system (3). This case provides a chronological presentation of COVID-19 following the diagnosis of primary infertility.

## Case Report

A 29-year-old male patient, with no co-morbidities and who was married for 1.5 years, had been admitted to the emergency department due to a fever at 39 °C, which had persisted for 3 days. The result of the quantitative reverse transcriptase-polymerase chain reaction analysis performed on a pharyngeal swab sample was positive. Laboratory analyses resulted in mild leukopenia of 3.789/mm<sup>3</sup>, hemoglobin of 14.3 g/dL, normal D-dimer of 0.2 mg/L, and ferritin of 65/μL. A urea of 24 mg/

dL, creatinine of 1.08 mg/dL, sodium of 138 mg/dL, potassium of 4.01 mEq/L, aspartate aminotransferase of 22 U/L, alanine aminotransferase of 15 U/L, fibrinogen of 352.1 g/L, total bilirubin of 0.5 mg/dL, and sedimentation of 2 mm/h were at a normal level. The C-reactive protein (CRP) was 5.62 mg/L (normal 5-10 mg/L). Favipiravir and enoxaparin sodium were administered. The semen analyses were evaluated according to the World Health Organization 2010 reference values. The pain was assessed according to the Wong-Baker face pain rating scale. The testes were examined with scrotal ultrasound/Doppler. The patient had oligo-astheno-teratozoospermia before the onset of COVID-19 (Table 1). The patient came to our clinic on day 45 after COVID-19. The semen analysis performed in an external center revealed a severe oligo-astheno-teratozoospermia that has developed on day 22 of COVID-19. Mild pain began on day 22 and intensified on day 49 in both testicles (+). Left testicular volume was lower compared to that of the right testis under ultrasound. The volume reduction in right and left testes occurred as 16.3/mm<sup>3</sup> (29.9/23.3 mm<sup>3</sup>, 25.41%) and 12.5/mm<sup>3</sup> (28.9/16.4 mm<sup>3</sup>, 43.25%), respectively, on day 49 (Figure 1). Orchialgia, which woke up the patient and was suppressed with paracetamol, developed on days 60 and 75, but no typical

**Correspondence:** Ahmet Salvarci MD, Novafertile and Medicana Hospital IVF Centers, Medicana Hospital Affiliated with KTO Medical Faculty, Department of Urology, Konya, Turkiye

**Phone:** +90 332 321 51 51 **E-mail:** drsalvarci@hotmail.com **ORCID-ID:** orcid.org/0000-0002-5231-2415

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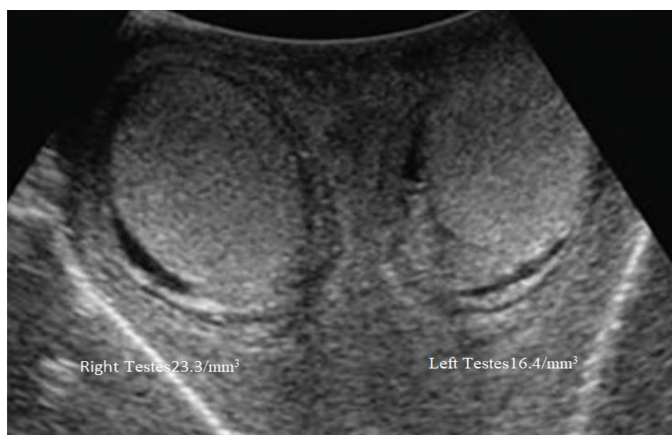
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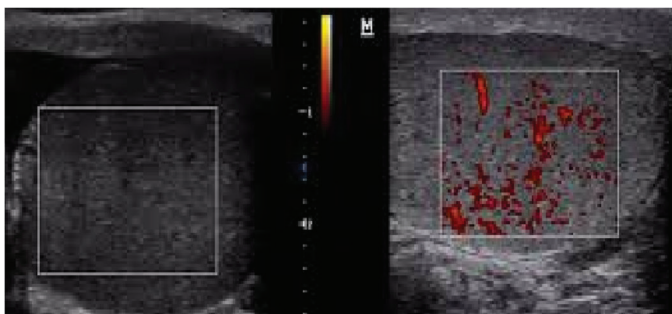
**Table 1. Chronological list evaluating the results before and after COVID-19**

2020-2021 year	22.01	23.01	01.06	19.09	11.10	14.10.2020	3.11	4.11	7.11	18.11/3.12	18.12	19-23/2021	4.1.2021	17.1.2021
	Before	Before	Before	Days 1,10,18	Day 22	Day 25	Day 45	Day 46	Day 49	Days 60,75	Day 90	Day 91-95	Day 108	Day 113
FSH mIU/L		2.42						2.6			2.98		2.7	
LH mIU/L		5.46						4.04			3.74		3.93	
PRL mIU/L		15.77						8.53			14.22		9.66	
E2 pg/mL								48.2					33.49	
TT ng/dL		303.57						395.26			216.44		173.89	
Volume/mL	5		4		3.5		4				5.2		3.6	
Number/mL	2.7x10 <sup>6</sup>		7x10 <sup>6</sup>		0.6x10 <sup>6</sup>		4x10 <sup>6</sup>				8x10 <sup>6</sup>		9x10 <sup>6</sup>	
Total count	13.5x10 <sup>6</sup>		28x10 <sup>6</sup>		2.1x10 <sup>6</sup>		16x10 <sup>6</sup>				41x10 <sup>6</sup>		32.4x10 <sup>6</sup>	
Rapidly progressive %	24		32		0		0				0		0	
Slowly progressive %	0		12		0		0				13		33	
In situ motile %	10		56		4		7				0		0	
Immotile %	66		44		96		93				87		67	
Kruger normal %	1		1		0		1				1		1	
TMSC	2.7x10 <sup>6</sup>		15.7x10 <sup>6</sup>		0.084x10 <sup>6</sup>		1.12x10 <sup>6</sup>				5.33x10 <sup>6</sup>		3.85x10 <sup>6</sup>	
Righ testis/ mm <sup>3</sup>		29.9, echo N			29.9, echo N				23.3, echo ↑, volume ↓	21.3, echo ↑, volume ↓			14, echo N, volume ↓	
Left testis/ mm <sup>3</sup>		28.9, echo N			28.9, echo N				16.4, echo ↑, volume ↓	15.7, echo ↑, blood flow ↑, volume ↓			12.2, still high echo, volume ↓	
Varicocele		2 mm, reflux (+)			2 mm reflux (+)						2 mm reflux (+)			
Righ W-B	0	0	0	0	2 or 4	2 or 4	2 or 4	2 or 4	2 or 4	8	0		Absent	
Left W-B	0	0	0	0	4	4	4	4	4	10	0		2	
qRT-PCR for COVID-19				<b>Positive</b>		<b>Negative</b>					<b>Negative</b>			
CRP mg/L					5.62			9.77		37.9	2.9		0.1	
ORP/mV/10 <sup>6</sup> sperm/mL			<b>0.98</b>		3.76		2.45				1.89		1.1	
SDFI (TUNEL)	8				22		26				11		8	
ICSI											<b>ICSI day</b>	Embryo transfer		
Time-lapse/h, division												42.9±27.88		<b>Pregnant</b>
Complete urine					N				<b>N</b>	<b>N</b>			N	
SPSS 27.0 program														

COVID-19: Coronavirus disease-2019, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, TT: Total testosterone, PRL: Prolactin, E2: Estradiol, LT: Liquefaction time, ICSI: Intracytoplasmic sperm injection, TMSC: Total motile sperm count, Wong-Baker (W-B) Face pain rating scale; 0 no hurt, 2 hurts little bit, 4 hurts little more, 6 hurts even more, 8 hurts whole lot, 10 hurts worst, qRT-PCR: Quantitative reverse transcriptase-polymerase chain reaction, CRP C-reactive protein, SDFI: Sperm DNA fragmentation, Time-lapse the system for monitoring early embryo morphokinetics development, B HCG shows pregnancy value in blood. The embryo is checked on the 12<sup>th</sup> day following the transfer. It indicates pregnancy between 5-50 mIU/mL in the first three weeks. TUNEL: The terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate-nick end labeling (TUNEL) assay, ORB: Oxidation-reduction potential (An ORB cut-off value of <1.42 mV/106 sperm/mL was regarded normal), N normal ↓ decreased, ↑ increased



**Figure 1.** Testicles with elevated echogenicity on day 49 due to COVID-19  
COVID-19: Coronavirus disease-2019



**Figure 2.** Elevated echogenicity in the right/left testes and elevated blood flow in the left testis under scrotal color Doppler on day 75 after COVID-19  
COVID-19: Coronavirus disease-2019

epididymitis orchitis swelling was observed. The patient's white blood cell count was (12.600/ $\mu$ L) with lymphocytopenia (724/ $\mu$ L). A reduction in testicular volumes was noted in both testes and particularly in the left testis under Doppler. The echogenicity was elevated. The left testicular blood flow was observed to increase (Figure 2). The semen values were consistent with the levels before COVID-19 from days 45 to 108. No changes occurred in the gonadotropic and prolactin values on days 46 to 90 before and after COVID-19; however, a decrease was observed in the total testosterone (TT) hypogonadism level on days 90 to 108. The patient had no pain in his right testis on day 108 during his follow-up, but the pain in his left testis persisted. A decrease was observed in the testicular volumes under ultrasound. His left testicular echogenicity was still elevated. The volume reduction in the right and left testes occurred as 15.9/ $\text{mm}^3$  (29.9/14  $\text{mm}^3$ , 53.17%) and 16.5/ $\text{mm}^3$  (28.7/12.2  $\text{mm}^3$ , 57.78%), respectively from days 49 to 108. Permanent losses were noted in rapidly progressive and *in situ* motile sperms in the semen analyses on day 108 (Table 1). An intracytoplasmic sperm injection (ICSI) was performed on day 90. Embryo transfer was carried out on day 95 and pregnancy was detected in the blood on day 113. Ultrasonographic gestational sac and fetal pulses were observed on day 131 after COVID-19. A healthy pregnancy of 8 weeks is

currently preserved. All chronological follow-up is presented in Table 1.

## Discussion

It was claimed that SARS-CoV-2 causes spermatogonia and increases expression in Leydig and Sertoli cells with angiotensin-converting enzyme 2 receptors and triggers an autoimmune inflammatory response (4). Autoimmune orchitis disrupts the testicular-blood barrier (3,4). This disrupts the balance of reactive oxygen species. The oxidative stress disrupts sperm morphology and acrosome structure and leads to damage in sperm deoxyribonucleic acid (DNA). Simultaneous elevation of oxidative reduction potential (ORP), CRP, and sperm DNA fragmentation index (SDFI) seemed to support COVID-19 autoimmune orchitis. Interestingly, normalization was observed in all three values towards day 108. We saw high-quality sperms with acrosome and high motility and cytoplasmic integrity, in which we detected the nuclei in intracytoplasmic morphologically selected sperm injection (IMSI). We observed embryo formations of 2PN (pronucleus) quality in our morphokinetic follow-ups in time-lapse on day 5. CRP elevations may negatively impact testicular functions and spermatogenic activity (4). CRP elevation, severe orchialgia, and increase in testicular echogenicity were observed on days 66 to 75, whereas a volume reduction was noted in the testes compared to day 49 (Figure 1, 2). Even if the body temperature increases by one degree, the regulation of the scrotal temperature is disrupted. Thus, sperm count and/or motility is/are reduced (5). This leads to a modification in the sperm DNA integrity (5). A minimum of 3 months may be required to normalize these parameters (6). Therefore, assisted reproductive approaches are recommended to be postponed for at least 3 months in men who have COVID-19 with fever (6). COVID-19 was reported to promote the negative impact of testosterone (7). Severe scrotal pain, elevation in testicular echogenicity, reduction in their volume, and a TT reduction signaling hypogonadism on days 90 through 108 were observed in our 3-month follow-up.

Despite being temporary, an elevation in CRP and ORP, high fever, and transiently rising SDFI levels were observed in the male patient with COVID-19. A severe reduction occurred in transient total sperm count, whereas a permanent reduction was noted in total motile sperm count levels. Testicular pain that developed after COVID-19 persisted for a long time. Most importantly, a permanent reduction occurred in testicular volumes. High-quality sperms were detected in IMSI. A high fertilization rate was achieved. Embryo morphokinetics was normal at time-lapse. Despite debated changes associated with COVID-19 in a male patient with primary infertility, ICSI that was performed 3 months after the disease resulted in pregnancy.

## Ethics

**Informed Consent:** Consent was obtained from the patient to use the data.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: A.S., A.S.G., F.A., Design: A.S., Data Collection or Processing: A.S., F.A., Analysis or Interpretation: A.S., Literature Search: A.S., A.S.G., F.A., Writing: A.S.

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