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Journal of Antivirals & Antiretrovirals

Research Article

The Effects of COVID-19 on Spermatogenesis

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ABSTRACT

Objective: To observe changes in sperm parameters after 72 days of infection by COVID-19.

Methods: A total of 100 patients had been enrolled in the study by a criteria suggesting good semen analysis. Two sets of semen analysis done, the first after 72 days of first positive swab for COVID-19 to show changes in the cycle of spermatogenesis during infection, the other sample after 72 days from the first to compare it with the first sample.

Results: A total number 100 patients first sample show 2% of patient's oligospermia, 36% of patient's teratospermia. The second sample shows 4% of patients' teratospermia. by comparing the two samples there is a significant increase in sperm concentration also a significant increase in motility (A+B), a highly significant increase in the normal forms of sperms.

Conclusion: COVID-19 affects spermatogenesis in the form of reversible teratospermia, reversible decrease sperm count but within normal level, reversible decrease in the sperm motility but also within normal level.

Keywords: COVID-19; Semen analysis; Spermatogenesis

Abbreviations: COVID-19: Coronavirus Disease 2019; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; ACE2: Angiotensin Converting Enzyme; RAAS: Renin Angiotensin Aldosterone System; RT-PCR: Reverse Transcription Polymerase Chain Reaction; LH: Luteinizing Hormone; HIV: Human Immunodeficiency Virus; AT1R: The Angiotensin II Type 1 Receptor; AG2R: Angiotensin-2 Receptor; PI3K: Phosphatidylinositol-3-Kinase; AKT: Serine/threonine kinase; ADAM: A Disintegrin And Metalloproteases; IL-6: Interleukin-6; CT: Computerized Tomography.

INTRODUCTION

The COVID-19, created by a new, exponentially evolving, mutated SARS-CoV-2, has become a major public health emergency worldwide [1]. Although the lungs are the key organ targeted in this disease, other vital organs may be involved, such as the heart and kidney. The main host receptor of the SARS-CoV-2 is ACE2, a major component of the RAAS. The ACE2 is also important in testicular male regulation of steroidogenesis and spermatogenesis. Since SARS-CoV-2 is capable of infecting the testis *via* ACE2 and adversely affecting the male reproductive system. A recent report published in JAMA Network Open revealed that in an analysis 38 semen samples from COVID-19 patients, 6 (four at the acute stage of infection and, alarmingly, two who were recovering) tested positive for the virus by RT-PCR [2].

Importantly, at this point, if the real virus was viable and contagious, we have no idea. However, additional data indicating that active COVID-19 infection significantly reduced the testosterone to LH ratio indicated the possibility that this coronavirus may have a pathophysiological effect on the studies, suggesting a major impact on the responsiveness of Leyding cells to LH stimulation. In several ways, these findings do not surprise us because, considering the large variety of pathogenic viruses (HIV, hepatitis, mumps, papilloma) that are known to be capable of destroying the testes and making the host infertile, the blood test barrier is known to offer little protection against viral invasion [3,4].

The angiotensin system plays a vital role in human spermatozoa's survival and functionality, but also creates a weakness to the attack of COVID-19. Angiotensin 1 is a biologically inactive decapeptide that in turn activates the AT1R and AG2R receptors, both of which are present in these cells, by cleaving ACE1 to generate angiotensin II. ACE2 is further processed by angiotensin II to produce angiotensin 1-7, which binds to the PI3K activating MAS receptor [5,6].

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Received: August 09, 2021; **Accepted:** August 23, 2021; **Published:** August 30, 2021

Citation: Kamel M, Moniem AA, Zarzour M, Kurkar A, Behnsawy (2021) The Effects of COVID-19 on Spermatogenesis. J Antivir Antiretrovir. S22:002.

The latter then phosphorylates AKT, which, by phosphorylating essential sperm apoptosis regulators such as BADD, maintains cell viability. As long as BAD is phosphorylated, it is held in abeyance by a 14-3-3 keeper protein. However, BAD dephosphorylates are released from their interaction with 14-3-3 if the PI3/AKT pathway is disrupted, and transfer to the mitochondria where it inactivates anti-apoptotic factors and facilitates the intrinsic apoptotic cascade. The spike protein on COVID-19 specifically targets ACE2 and in so doing removes an essential stimulus for PI3K/AKT, thereby compromising sperm viability. Subsequent to COVID-19 attachment, the ectodomain of ACE2 may be removed by ADAM proteases and shed from the sperm surface. Alternatively, proteases from the TMPRSS family may promote fusion between the virus and the sperm surface, either as intrinsic components of the sperm plasma membrane or provided by seminal proteasomes, by cleaving ACE2 and the viral spike proteins (S1 and S2) at the sites indicated by dashed lines, thereby completing the transformation of this cell from procreating gamete to viral vector [7,8].

Fever is an added risk in the COVID-19 pandemic that could affect male fertility. An important manifestation of the COVID-19 pandemic is an especially high and prolonged rise in body temperature, complicating more than 80 percent of patients. The belief that fever and testicular temperature elevation result in spermatogenesis deficiency is generally accepted.

More importantly, emerging evidence suggests that secondary cytokine storm syndrome can occur in a subgroup of patients with extreme COVID-19 (hemophagocytic lymphohistiocytosis). This is a hyper inflammatory, under recognized syndrome characterized by sustained fever.

With fulminant and fatal hypercytokinemia with multiorgan failure. With cytopenia and hyperferritinemia, these patients have a clear serum blood cytokine profile. These results also indicate that immunomodulatory therapy (IL-6 antagonist) in these patients will dramatically increase mortality rates [9].

Since cytokines contribute to the testicular function and preservation of male reproductive health and to the pathologies associated with their irregular organ activity, changes in the cytokine profile caused by COVID-19 may have additional consequences for male fertility. Furthermore, immunomodulatory therapies may have possible long-term effects on male fertility and are a matter of concern. In addition, cytokine microenvironment variations within the testis can have tumorigenic cellular adverse effects, potentially contributing to testicular cancer, a second long-term problem of concern [5,9,10].

METHODOLOGY

Our observational study conducted on 100 patients infected by COVID-19 and we obtained two semen analyses, the first after 72 days of first positive swab for COVID-19 and the other sample after 72 days from the first sample at Assiut university hospital after written informed consent was obtained from each participant in the study.

Inclusion criteria were patients younger than 45 years old, no history of fertility disorders (if married history of conception), normal secondary sexual character, CT chest normal to decrease the effect of stress and no hypoxia.

Exclusion criteria were patients had congenital anomalies of the testis. Chronically ill patients (diabetic-hypertensive-cardiac). Males with varicocele. Patients with special habits (smoking, drinking alcohol).

All cases that fulfill the selection criteria (non-probability sample size) with expected size of 100 patients starting from 01/01/2020 to 20/5/2021.

Patients whose follow-ups will be lost because of death or any other cause will be excluded from this study (expected to be 25%).

All patients were subjected to full history taking, general examination and laboratory examination (semen analysis).

Two sets of semen analysis done, the first after 72 days of first positive swab for COVID-19 to show changes in semen analysis from normal values in the cycle of spermatogenesis during infection, the other sample after 72 days from the first sample to show if the changes regress to normal and to compare it with the first sample.

Research outcome measures

Changes of semen parameter after 72 days of infection by COVID-19. Follow up semen analysis after 72 days of the first sample to see if it's permanent change and to compare with the first sample.

RESULTS

There was highly statistically significant difference found between First semen analysis and Second semen analysis Regarding Morphology (normal forms) %, and there was statistically significant difference found between First semen analysis and Second semen analysis Regarding Sperm concentration (ml) and Motility (A+B) %, and there was no statistically significant difference found between first semen analysis and second semen analysis Regarding PH, Volume, RBCs and Pus cell (Tables 1 and 2).

The Previous table shows that there was highly statistically significant difference found between first semen analysis and second semen analysis regarding morphology (normal forms)%, and there was statistically significant difference found between first semen analysis and second semen analysis regarding sperm concentration (ml) and motility (A+B) %, and there was non-statistically significant difference found between first semen analysis and second semen analysis regarding PH, Volume, RBCs and Pus cell.

DISCUSSION

A total number 100 patients with mean (age 24.6, BMI 25.97), with no comorbidity with criteria mentioned before (Table 1). First sample show 2% of patients oligospermia, 36% of patients teratospermia (Table 2). The second sample shows 4% of patient's teratospermia (Table 2). By comparing the two samples there is a significant increase in sperm concentration with mean concentration in the first sample 96.49 million/ml, mean concentration in the second sample 104.67 million/ml, a significant increase in motility (A+B) with mean percentage of 44% in the first sample and 46% in the second sample, a highly significant increase in the normal forms of sperms with mean percentage of 23.4% in the first sample and 30.55% in the second sample (Table 2).

Table 1: Distribution of the studied cases according to age, length, weight, BMI, DM, HTN, cardiac, special habit, other and previous surgery.

		No=100
Age	Mean ± SD	24.61 ± 3.34
	Range	21-35
Length	Mean ± SD	1.71 ± 0.06
	Range	1.5-1.78
Weight	Mean ± SD	75.42 ± 10.41
	Range	55-99
BMI	Mean ± SD	25.97 ± 3.73
	Range	18.59-37.11
DM	No	100 (100.0%)
HTN	No	100 (100.0%)
Cardiac	No	100 (100.0%)
Special habit	No	100 (100.0%)
Other	No	100 (100.0%)
Previous surgery	No	100 (100.0%)

Table 2: Comparison between first semen analysis and second semen analysis regarding PH, volume, sperm concentration (ml), motility (A+B) %, morphology (normal forms) %, RBCs and Pus cell.

Semen analysis		First	Second	Paired t-test	P-value	Sig.
PH	Mean ± SD	7.63 ± 0.26	7.61 ± 0.26	0.554	0.581	NS
	Range	7-8	7-8			
Volume	Mean ± SD	3.27 ± 0.75	3.25 ± 0.76	0.237	0.813	NS
	Range	2-4.6	2-4.6			
Sperm concentration (ml)	Mean ± SD	96.49 ± 35.87	104.67 ± 33.80	-1.871	0.054	S
	Range	12-154	15-154			
Motility (A+B) %	Mean ± SD	44.52 ± 6.67	46.47 ± 7.09	-0.047	0.043	S
	Range	34-58	34-58			
Morphology(normal forms)	Mean ± SD	23.41 ± 17.64	30.55 ± 12.98	-7.035	0	HS
	Range	1-55	2-60			
RBCs	Mean ± SD	1.07 ± 0.78	1.06 ± 0.76	0.107	0.915	NS
	Range	0-2	0-2			
Pus cell	Mean ± SD	1.20 ± 0.99	1.07 ± 0.76	0.935	0.352	NS

P-value >0.05: Non Significant (NS); P-value <0.05: Significant (S); P-value<0.01: Highly Significant (HS).

*: Paired t-test.

CONCLUSION

COVID-19 affects spermatogenesis in the form of reversible teratospermia, reversible decrease sperm count but within normal level, reversible decrease in the sperm motility but also within normal level.

DECLARATIONS

Acknowledgment

Nil

CONFLICT OF INTEREST

None declared

ETHICAL CONSIDERATION

Our observational study conducted on 100 patients after approved by Assiut University Institutional Review Board and written informed consent was obtained from each participant in the study.

Approval of the research protocol by an institutional reviewer board

(N/A)

Informed consent

It was obtained from each participant in the study.

Registry and the registration no. of the study

(N/A)

REFERENCES

1. Abobaker A, Raba AA. Does COVID-19 affect male fertility? World J Urology. 2021;39:975-976.
2. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020;181:271-280.

3. Nascimento BIJ, Cacic N, Abdulazeem HM, von Groote TC, Jayarajah U, Weerasekara I, et al. Novel coronavirus infection (COVID-19) in humans: A scoping review and meta-analysis. J Clin Med. 2020;9:941.

4. Carlsen E, Andersson AM, Petersen JH and Skakkebaek NE. History of febrile illness and variation in semen quality. Hum Reprod. 2003;18:2089-2092.

5. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy Region, Italy. JAMA. 2020;323:1574-1581.

6. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. 2020;382:1708-1720.

7. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell. 2020;181:281-292.

8. Xu J, Qi L, Chi X, Yang J, Wei X, Gong E, et al. Orchitis: A Complication of Severe Acute Respiratory Syndrome (SARS). Biol Reprod. 2006;74:410-416.

9. Segars J, Katler Q, McQueen DB, Kotlyar A, Glenn T, Knight Z, et al. Prior and novel coronaviruses, Coronavirus Disease 2019 (COVID-19), and human reproduction: What is known? Fertility Sterility. 2020;113:1140-1149.

10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395:497-506.