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Influence of COVID-19 on Male Fertility

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Abstract

Background: Coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may lead to the significant changes of spermogramme.
Objectives: This study aimed to investigate the impact of COVID-19 infection on sperm parameters in fertile men.
Methods: A total of 30 males were selected and divided into two groups: (1) 1) Patients who were not infected with Covid-19, a total of 10 patients. (2) Patients who were infected with COVID-19. Semen and nasal swab samples were gathered from all subjects. COVID-19 was detected via RT-PCR. Semen analysis, DNA fragmentation, and sperm bacteriology were assessed.
Results: Results demonstrated that sperm concentration, motility, sperm viability, and DNA fragmentation were significantly reduced in males with virus infection. In comparison with the control group, ($P < 0.05$). Data indicated that the semen volume was not significantly correlated with COVID-19, and there was a significantly negative correlation between sperm concentration, sperm total motility, sperm vitality, sperm normal forms. Sperm DNA fragmentation index had a significant and positive correlation with COVID-19 ($P < 0.05$). In addition, reproductive hormones significantly reduced in fertile males with COVID-19 infection ($P < 0.05$).
Conclusions: COVID-19 infection has a negative influence on sperm parameters in males.

Keywords – COVID-19; coronavirus; semen; sperm quality, DNA fragmentation.

I. INTRODUCTION

Currently, the coronavirus disease 2019 (COVID-19) infection is threatening human health worldwide, causing acute damages in the vital organ systems (lungs, kidneys, and heart) (1). Coronavirus is divided into 46 different species and has been detected in animals and humans (2). After December 2019, COVID-19 infection increased in the world and caused concerns about the probable effect of COVID-19 on reproductive organs and the fertility of males. It was reported that over 25 viruses could enter human semen and negatively affect spermatozoa or male fertility (3), such as herpes simplex virus (HSV) and human immunodeficiency viruses (HIV) (4). It is critical to know whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) could have the same effect on males, and this was not answered in a preliminary investigation (5). COVID-19 might induce male infertility by direct viral replication and viral dissemination-induced cytopathic effects in the testis and indirect immunopathology-caused male fertility harm (6). Findings from some studies show that the coronavirus can directly affect testicular tissue and some sperm parameters by altering the expression pattern of the angiotensin-converting enzyme 2 (*ACE2*) gene (7, 8). In fact, seminiferous duct cells, spermatogonia, Leydig cells, and Sertoli cells being four testis-specific cell types, express this enzyme (8). In a study by Nikolayeva et al., it was found that the *ACE* enzyme is located in sperm, mostly in the post-

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acrosomal region, neck, and middle of normal sperm (7). *ACE* expressed in sperm binds glycosylphosphatidylinositol (GPI) proteins to the zona pellucida region, which ultimately leads to the fertilization process (9). Furthermore, previous studies (10, 11) have demonstrated that *ACE* activity is associated with human male fertility. In addition, there is also the hypothesis that binding SARS-CoV-2 to the *ACE2* receptor increases *ACE2* activity in sperm cells and the side effects in fertilization owing to abnormal functions of sperm cells (8, 12, 13). Various studies have shown that the virus and its infections reduce the rate of sex hormones (14, 15). Because testosterone is one of the most important hormones in male reproduction, the reduction of its level will have adverse effects on male fertility and germ cell survival (16). Thus, changes in reproductive hormone levels caused by COVID-19 infection can reduce male fertility (15).

II. Material and Methods

The study was conducted in August-September 2020. It included 30 participants, aged 18-40, who were not vaccinated with the COVID-19 vaccine and had a normal sperm analysis.

Study participants were divided into 2 groups:

1) Patients who have not had COVID-19 (10 patients)

2) Patients who have had COVID-19 with variable severity (20 patients)

Group 2 included patients who had COVID-19 and were diagnosed with a PCR test of the nasopharyngeal swab (COVID-19 PCR test uses primers that match the segment of the viral genome. This way, multiple copies of this sample can be produced and used to find out if the patient has COVID-19). The sperm analysis microscopically (sperm concentration in 1 mL semen; percentage of motile spermatozoa; concentration of functionally active and progressively motile spermatozoa) as well as with analyzer (sperm quality analyzer SQAIIC-P Israel method) was performed in parallel with COVID-19 PCR testing. Additionally, a bacteriological investigation of sperm was performed with a manual method using API systems. Lastly, sperm DNA fragmentation with the SCD method was done. This latter is based on DNA denaturation that removes all the spermatozoal proteins and reveals loops of DNA fibers, also known as a halo. This method enables data interpretation in percentages.

Based on the patient history, group 2 was further divided into 5 subgroups:

1) Asymptomatic patients with positive COVID-19 PCR result - 2 patients

2) Patients with subfebrile temperature and anosmia but no need for hospitalization - 7 patients

3) Hospitalized patients with moderate severity of COVID-19, mild resistance to treatment, fever, anosmia, and fatigue. CT scan of lungs revealed ground-glass opacity (opacity 5-8%) – 4 patients

4) Hospitalized patients on CPAP with variable symptoms, fever, cough, anosmia, fatigue, and shortness of breath – 6 patients

5) Patients admitted to ICU due to shortness of breath without the need for mechanical ventilation) – 1 patient

III. Results

Asymptomatic COVID-19 patients and those with the subfebrile temperature and anosmia (a total of 7 patients) had normal sperm count but reduced sperm motility parameters, the phenomenon known as asthenospermia. The concentration of progressively motile spermatozoa was reduced twice the normal count. Bacteriological investigation of sperm revealed gram-negative rods Escherichia coli 10^4 CFU/ml (3 patients) and Enterobacter cloacae 10^5 CFU/ml (2 patients) as well as Staphylococcus aureus 10^4 CFU/ml (2 patients). 2 patients had no growth of pathogenic microorganism. However, the DNA fragmentation index was less than 15%.

Bacteriological investigation of sperm in hospitalized patients with fever, anosmia, oxygen dependence, and ground-glass opacity on CT (10 patients), revealed Enterococcus faecalis 10^6 CFU/ml (4 patients), Staphylococcus aureus 10^7 CFU/ml (3 patients), Escherichia coli 10^5 CFU/ml (2 patients). 1 patient had no microbial growth.

DNA fragmentation index ranged from 15% to 30%. Sperm analyzer revealed oligoasthenoteratozoospermia in all these patients.

The patient hospitalized in ICU had azoospermia. Bacteriological examination of sperm showed Enterobacter aerogenes 10^8 CFU/ml. DNA fragmentation index ranged from 30% to 40%.

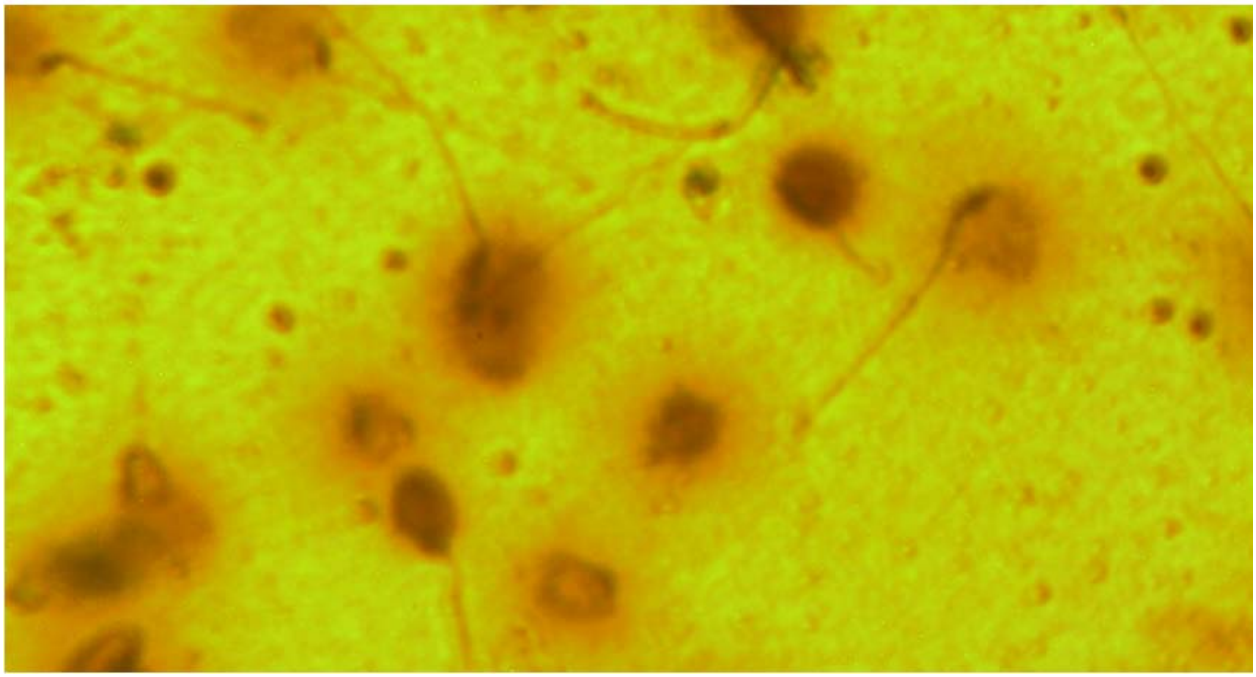

Figure 1. Microphotograph of sperm DNA fragmentation before COVID-19 infection. Prominent halos around spermatozoal heads indicate healthy spermatozoa.

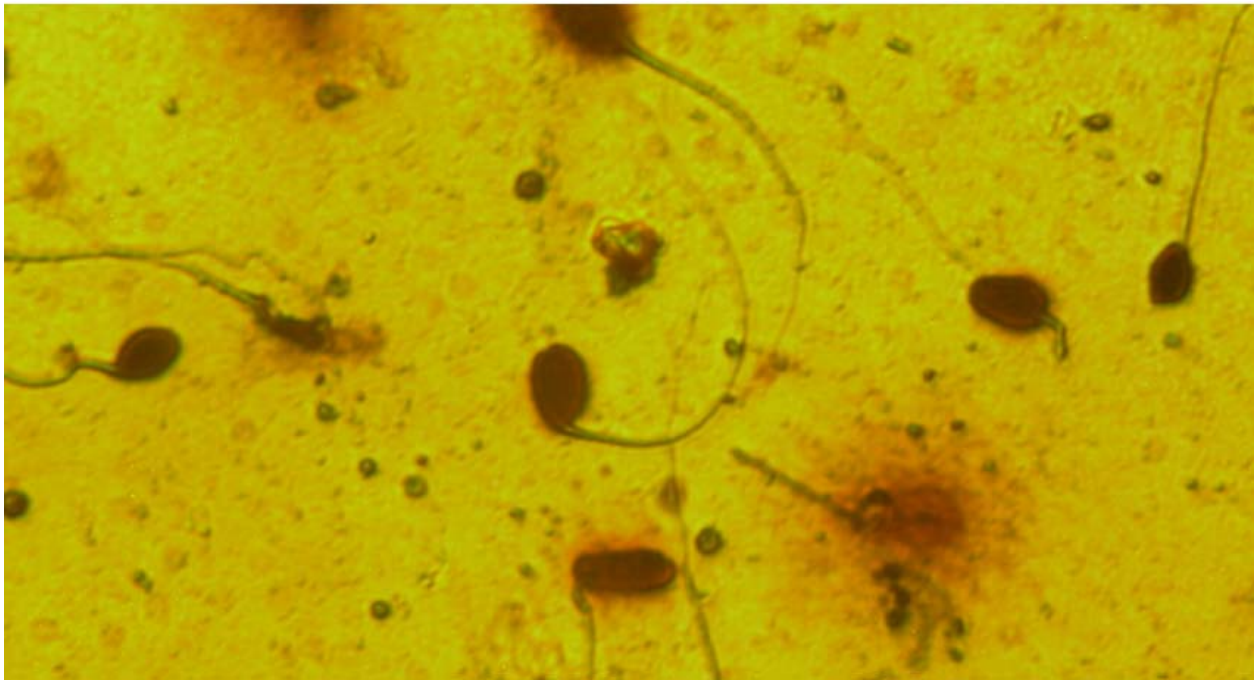

Figure 2. Microphotograph of sperm DNA fragmentation after COVID-19 infection. The absence of halos around spermatozoal heads indicates DNA fragmentation.

IV. Conclusion:

This study showed that COVID-19 has a significant impact on spermatogenesis regardless of the severity of clinical presentation. There is a negative effect on sperm in all patients with variable severity of COVID-19 infection evidenced by our study groups. It is known that any viral infection accompanied by high fever can hinder spermatogenesis.

It is worth noting that change in spermogramme may be caused by inflammation itself or specifically by COVID-19. This topic is still a matter of investigation that needs clinical observation and assessment as well as short and long-term prognosis.

References

[1] Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;**579**(7798):270-3. doi: 10.1038/s41586-020-2012-7. [PubMed: 32015507]. [PubMed Central: PMC7095418].

[2] Helmy YA, Fawzy M, Elaswad A, Sobieh A, Kenney SP, Shehata AA. The COVID-19 pandemic: A comprehensive review of taxonomy, genetics, epidemiology, diagnosis, treatment, and control. *J Clin Med*. 2020;**9**(4). doi: 10.3390/jcm9041225. [PubMed: 32344679]. [PubMed Central: PMC7230578].

[3] Salam AP, Horby PW. The breadth of viruses in human semen. *Emerg Infect Dis*. 2017;**23**(11):1922-4. doi: 10.3201/eid2311.171049. [PubMed: 29048276]. [PubMed Central: PMC5652425].

[4] Klimova RR, Chichev EV, Naumenko VA, Gadzhieva ZS, Tsibisov AS, Adieva AA, et al. [Herpes simplex virus and cytomegalovirus in male ejaculate: herpes simplex virus is more frequently encountered in idiopathic infertility and correlates with the reduction in sperm parameters]. *Vopr Virusol*. 2010;**55**(1):27-31. Russian. [PubMed: 20364668].

[5] Paoli D, Pallotti F, Turriziani O, Mazzuti L, Antonelli G, Lenzi A, et al. SARS-CoV-2 presence in seminal fluid: Myth or reality. *Andrology*. 2021;**9**(1):23-6. doi: 10.1111/andr.12825. [PubMed: 32453494]. [PubMed Central: PMC7283802].

[6] Aitken RJ. COVID-19 and human spermatozoa-Potential risks for infertility and sexual transmission? *Andrology*. 2021;**9**(1):48-52. doi: 10.1111/andr.12859. [PubMed: 32649023]. [PubMed Central: PMC7404878].

[7] Nikolaeva MA, Balyasnikova IV, Alexinskaya MA, Metzger R, Franke FE, Albrecht R2, et al. Testicular isoform of angiotensin I-converting enzyme (ACE, CD143) on the surface of human spermatozoa: revelation and quantification using monoclonal antibodies. *Am J Reprod Immunol*. 2006;**55**(1):54-68. doi: 10.1111/j.1600-0897.2005.00326.x. [PubMed: 16364013].

[8] Verma S, Saksena S, Sadri-Ardekani H. ACE2 receptor expression in testes: implications in coronavirus disease 2019 pathogenesisdagger. *Biol Reprod*. 2020;**103**(3):449-51. doi: 10.1093/biolre/ioaa080. [PubMed: 32427288]. [PubMed Central: PMC7314215].

[9] Li LJ, Zhang FB, Liu SY, Tian YH, Le F, Wang LY, et al. Human sperm devoid of germinal angiotensin-converting enzyme is responsible for total fertilization failure and lower fertilization rates by conventional in vitro fertilization. *Biol Reprod*. 2014;**90**(6):125. doi: 10.1095/biolreprod.113.114827. [PubMed: 24790158].

[10] Foresta C, Mioni R, Rossato M, Varotto A, Zorzi M. Evidence for the involvement of sperm angiotensin converting enzyme in fertilization. *Int J Androl*. 1991;**14**(5):333-9. doi: 10.1111/j.1365-2605.1991.tb01101.x. [PubMed: 1665481].

[11] Shibahara H, Kamata M, Hu J, Nakagawa H, Obara H, Kondoh N, et al. Activity of testis angiotensin converting enzyme (ACE) in ejaculated human spermatozoa. *Int J Androl*. 2001;**24**(5):295-9. doi: 10.1046/j.1365-2605.2001.00301.x. [PubMed: 11554987].

[12] Chen YW, Lee MS, Lucht A, Chou FP, Huang W, Havighurst TC, et al. TMPRSS2, a serine protease expressed in the prostate on the apical surface of luminal epithelial cells and released into semen in prostasomes, is misregulated in prostate cancer cells. *Am J Pathol*. 2010;**176**(6):2986-96. doi: 10.2353/ajpath.2010.090665. [PubMed: 20382709]. [PubMed Central: PMC2877858].

[13] Li D, Jin M, Bao P, Zhao W, Zhang S. Clinical characteristics and results of semen tests among men with coronavirus disease 2019. *JAMA Netw Open*. 2020;**3**(5). e208292. doi: 10.1001/jamanetworkopen.2020.8292. [PubMed: 32379329]. [PubMed Central: PMC7206502].

[14] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of Coronavirus disease 2019 in China. *N Engl J Med*. 2020;**382**(18):1708-20. doi: 10.1056/NEJMoa2002032. [PubMed: 32109013]. [PubMed Central: PMC7092819].

[15] Holtmann N, Edimiris P, Andree M, Doehmen C, Baston-Buest D, Adams O, et al. Assessment of SARS-CoV-2 in human semen-a cohort study. *Fertil Steril*. 2020;**114**(2):233-8. doi: 10.1016/j.fertnstert.2020.05.028. [PubMed: 32650948]. [PubMed Central: PMC7256599].

[16] Rastrelli G, Di Stasi V, Inglese F, Beccaria M, Garuti M, Di Costanzo D, et al. Low testosterone levels predict clinical adverse outcomes in SARS-CoV-2 pneumonia patients. *Andrology*. 2021;**9**(1):88-98. doi: 10.1111/andr.12821. [PubMed: 32436355]. [PubMed Central: PMC7280645].