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The Potential Impact of COVID-19 on Male Reproductive Health

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Abstract

Since the beginning of 2020, the whole world is trying to face the coronavirus disease 2019 (COVID-19) pandemic. In the last years, SARS-CoV-2 mutations showed an increased contagion and infection profile, affecting a higher proportion of young men during the last pandemic outbreaks. SARS-CoV-2 penetrates host cells by binding to Angiotensin-Converting Enzyme (ACE2) receptors, highly expressed by testis cells, and a significant hyper-gonadotropic hypogonadism rate in COVID-19 patients has been observed, leading to the hypothesis of a possible impact of this disease on male fertility. Indeed, recent founding demonstrated that 25% of patients healed by COVID-19 showed azoo/oligozoo-spermia. Moreover, a statistically significant decrease of sperm concentration, total number and sperm motility was detected in men with moderate infections, when compared with mild symptomatic men or controls. Thus, pathological levels of inflammatory cytokines in semen of men healed from COVID-19 were reported in a major percentage of studied men, with a significant correlation between oligo-crypto-azoospermia and disease severity. Even if the whole mechanisms of male reproductive damages are still unclear, autoimmune self-maintained inflammation may be one of the main determinants of male reproductive system impairment.

Keywords: ACE2; Men; Covid-19; Reproductive health; Hypogonadism; Sperm motility; Pandemic; SARS-CoV-2; Semen; Spermiogram

Short Communication

Since the beginning of 2020 the whole world is trying to cope with the coronavirus disease 2019 (COVID-19) pandemic. The new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in Wuhan (China) in late-December 2019 and it quickly spread around the world. Several new public health strategies have been implemented over the past 2 years to defeat the pandemic, such as partial or total lockdowns, wearing facemasks in public, social distancing, but above all effective vaccines against COVID-19, [1]. Nevertheless, viral mutations and/or environmental factors led to recurrent pandemic outbreaks all over the world, appointing COVID-19 as a still current major worldwide concern. Indeed, SARS-CoV-2 variants showed an increased infection profile. A higher percentage of younger men, more prone to paternity, was infected during the last pandemic outbreaks, as compared with the first one [2]. Thus, raising concerns about the possible impact of COVID-19 on male fertility.

SARS-CoV-2 penetrates host cells by binding to the Angiotensin-Converting Enzyme (ACE2) receptors with its spike protein. Somatic and germ cells of the testis express high levels of ACE2 and TMPRSS2, the starter of SRAS-Cov-2 spike protein, suggesting a potential viral concentration inside male gonads [3]. Moreover, it has been hypothesized a possible impairment of Leydig cell function in men with acute SARS-CoV-2 infection, observing a significant hyper-gonadotropic hypogonadism rate in these patients and suggesting a following alterations of semen quality in men affected by COVID-19 [4]. Indeed, recent founding from the first prospective study evaluating semen quality in men healed from COVID-19, demonstrated that 25% of healed COVID-19 patients showed azoo/oligozoo-spermia, a percentage evidently greater than that reported in the overall population [5]. Thus, over 43 patients evaluated at least 30 days after the second negative nasopharyngeal swab for SARS-COV-2, semen analysis revealed that three patients had less than 2 million/mL (7.0%) of spermatozoa and eight patients (18.6%) were crypto/azoospermic, and azoospermia was stringently related with COVID-19 severity. Even if a spermiogram was not available before COVID-19, the authors reported that all the azoospermic patients had children [5].

Furthermore, a statistically significant decrease of sperm concentration, sperm total number per ejaculate, overall and

progressive sperm motility was observed in men with moderate infections, when compared with mild symptomatic men or controls [6]. Nevertheless, the presence of SARS-CoV-2 genome in semen, during the acute COVID-19 phase or after healing, was found only in a very small number of men enrolled in clinical studies [5,7]. The detrimental consequences on multiple organs and systems of SARS-CoV-2, including the male genitourinary system, have been widely described. Several studies investigated the pathophysiology and the inflammatory impact of COVID-19 on male genitourinary tract, urine and semen [5]. Some Authors reported the loss of epithelial-endothelial barrier integrity and edema with consequent impairment of oxygen diffusion, beyond the direct cellular inflammatory response against the virus [8].

Indeed, pathological levels of IL-8 in semen were reported in 76.7% of men healed from COVID-19, with a significant correlation between oligo-crypto-azoospermia and disease severity [5]. Moreover, a post-hoc analysis showed high levels of IL-6 and TNF-alfa both at one month from proven healing and at further follow-up with a consequent evidence of spermatogenesis impairment. Cytokines levels were consistently higher in men who showed a more severe impairment. Actually, IL-6 levels were almost twice in cryptoazoospermic patients compared with normozoospermic (164pg/ml (141-204) *vs.* 88pg/ml (45-186)), despite not being statistically significant, while TNF-alfa nearly reached a statistically significant difference (246pg/ml (208-329) *vs.* 208pg/ml (201-228); p=0.09). However, IL-1 was significantly higher in criptoazoospermic when compared to normozoospermic patients (116pg/ml (103-160) *vs.* 95pg/ml (94-99); p=0.01) [9].

These data are in line with the effect of semen inflammation evaluated in pre-COVID-19 era. Thus, cytokines levels in seminal plasma have been previously related to spermatogenesis impairment due to a damage to blood-testis barrier, in particular the impact of IL-6 and TNF-alfa on male fertility has been previously well proven [5,10]. Lamb et al. [11] evaluated the inflammatory impact on COVID-19 on genitourinary system by collecting urine in patients with COVID-19 associated cystitis [11], in comparison with healthy controls. All COVID-19 patients had elevated levels of inflammatory cytokines including IL-6, IL-8, and IP-10 in their urine while COVID-19 negative controls don't. Nevertheless, SARS-CoV-2 genome was found only in a negligible number of patients with symptomatic COVID-19 [12].

There are still limited data regarding the long-term impact on male reproductive health in patients recovered from COVID-19. Overall, the risk of transmission of SARS-CoV-2 through the semen or urine of men infected with COVID-19 seems negligible. Nevertheless, male fertility could be altered by COVID-19 driven inflammation of male accessory glands, in particular in patients healed after a moderate to severe COVID-19. Even if the whole mechanisms of male reproductive damages are still unclear, persistent high temperature and autoimmune self-maintained inflammation may be the main determinant of severe impairment of male reproductive system. Therefore, further preclinical and clinical studies are urgently needed to better understand the impact of SARS-CoV-2 infection and COVID-19 on male reproductive function, above all of younger men. Indeed, new diagnostic and therapeutic strategies could emerge for a better management of COVID-19 recovered men.

References

1. Morselli S, Liaci A, Nicoletti R, Pecoraro A, Gemma L, et al. (2020) The use of a novel smartphone app for monitoring male luts treatment during the COVID-19 outbreak. Prostate Cancer Prostatic Dis 23(4): 724-726.
2. Seligmann H, Iggui S, Rachdi M, Vuillerme N, Demongeot J (2020) Inverted covariate effects for first *versus* mutated second wave covid-19: high temperature spread biased for young. Biology (Basel) 9(8): 226.
3. Wang Z, Xu X (2020) scRNA-seq profiling of human testes reveals the presence of the ace2 receptor, a target for sars-cov-2 infection in spermatogonia, leydig and sertoli Cells. Cells 9(4): 920.
4. Rastrelli G, Di Stasi V, Inglese F, Beccaria M, Garuti M, et al. (2021) Low testosterone levels predict clinical adverse outcomes in SARS-CoV-2 pneumonia patients. Andrology 9(1): 88-98.
5. Gacci M, Coppi M, Baldi E, Sebastianelli A, Zaccaro C, et al. (2021) Semen impairment and occurrence of SARS-CoV-2 virus in semen after recovery from COVID-19. Hum Reprod 36(6): 1520-1529.
6. Holtmann N, Edimiris P, Andree M, Doehmen C, Baston-Buest D, et al. (2020) Assessment of SARS-CoV-2 in human semen-a cohort study. Fertil Steril 114(2): 233-238.
7. Li D, Jin M, Bao P, Zhao W, Zhang S (2020) Clinical characteristics and results of semen tests among men with coronavirus disease 2019. JAMA Netw Open 3(5): e208292.
8. Elterman D, Baard J, Averbeck MA, Hassouna M, Takahashi S, et al. (2021) Management of men with lower urinary tract symptoms due to benign prostatic hyperplasia during and after COVID-19. Societe Internationale d'Urologie J 2(6): 370-379.
9. Morselli S, Sebastianelli A, Liaci A, Zaccaro C, Pecoraro A, et al. (2019) Male reproductive system inflammation after healing from coronavirus disease 2019. Andrology.
10. Zhang H, Yin Y, Wang G, Liu Z, Liu L, et al. (2014) Interleukin-6 disrupts blood-testis barrier through inhibiting protein degradation or activating phosphorylated ERK in Sertoli cells. Sci Rep 4: 4260.
11. Lamb LE, Dhar N, Timar R, Wills M, Dhar S, et al. (2020) COVID-19 inflammation results in urine cytokine elevation and causes COVID-19 associated cystitis (CAC). Med Hypotheses 145: 110375.
12. Kashi AH, De la Rosette J, Amini E, Abdi H, Fallah-Karkan M, et al. (2020) Urinary viral shedding of COVID-19 and its clinical associations: a systematic review and meta-analysis of observational studies. Urol J 17(5): 433-441.

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