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P-091 Semen parameters and male reproductive potential are not negatively affected after recovery from COVID-19 disease

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Study question: Does COVID-19 disease negatively impact on male fertility after adequate time of recovery?

Summary answer: COVID-19 disease did not impact on semen parameters and male reproductive potential in infertile patients, when semen was collected at least three months after recovery

What is known already: The male reproductive system may be a potential target for SARS-CoV-2 since the presence of ACE and TMPRSS2 receptors. After a first report of the presence of SARS-CoV-2 in semen of COVID-19 patients, several papers reported that SARS-CoV-2 was not detected in the semen. However, some evidences indicated that COVID-19 disease could impair semen parameters. During the infection, or in a short period after, a reduction in sperm concentration (up to cases of azoospermia) and motility and an increase in DNA fragmentation were observed. There are no conclusive data exploring if these damages persist.

Study design, size, duration: In this longitudinal prospective study, performed at a tertiary level public fertility center from February 2020 to December 2021 we enrolled 20 men who had COVID-19 disease (1 severe, 15 mild/moderate, and 4 asymptomatic). We compared sperm parameters in semen samples collected before COVID-19 and at least three months after recovery (median=6 months, IQR 4-9). We also evaluated the reproductive potential of 18 men who performed ART cycles after the recovery.

Participants/materials, setting, methods: For each man we compared semen parameters before the COVID-19 disease and at least three months after recovery. Semen samples were analyzed following WHO guidelines. Medians and interquartile ranges (IQRs) were reported. The impact of COVID-19 on endpoints (semen volume, concentration, motility) was evaluated by Wilcoxon rank sum test. A subset of 18 patients performed ART cycles after COVID-19 recovery. Outcomes of these cycles were compared with reference performance indicators set at our center.

Main results and the role of chance: Comparing median semen volume and progressive motility before (2.9 ml, IQR 2.0-3.5; 38.5%, IQR 30.0-52.5) and after COVID-19 (2.5 ml, IQR 2.0-3.6; 40%, IQR 30.0-47.5) we did not find any statistical difference ($p=0.766$ and $p=0.782$, respectively). We

observed an improvement of median sperm concentration after disease recovery (before COVID-19: 26.0 million/ml, IQR 16-37, after: 68.0 million/ml, IQR 29.5-93.5, $p=0.003$), which may be due to intra-individual variability and to patients' management at our center (i.e., oral antioxidant treatments, other therapies, higher ejaculatory frequency). On the whole, semen parameters did not worsen although the median age of patients obviously increased (36.5 years, IQR 33.8-38 versus 37.5 years, IQR 35.9-39.6). Eighteen couples performed 29 ART cycles after recovery from COVID-19 disease of the male partners (12 IUI, 8 FIVET, 9 ICSI of which one from frozen oocytes). Fertilization, cleavage and top-quality rates were within the normal reference ranges of our center. A total of 6 clinical pregnancies were achieved (5 singletons and 1 twin). One gestation ended in a successful healthy newborn, whereas the remaining 5 pregnancies are ongoing. A total of 10 blastocysts were vitrified in 4 cycles, thus further embryo transfers will be performed.

Limitations, reasons for caution: The main limitations of the study are: small sample size, limited generalizability because no data were collected in fertile patients.

Wider implications of the findings: Our data are reassuring about the effect of COVID-19 disease on male fertility, if semen samples are collected at least three months after recovery from infection.

Trial registration number: not applicable