

## ESHRE 2022 / Oral presentations

## INVITED SESSION

## SESSION 01: KEYNOTE SESSION

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Gold

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**O-001 Semen impairment and occurrence of SARS-CoV-2 virus in semen after recovery from COVID-19**

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**Background:** The presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in human semen and its role in virus contagion and semen quality after recovery from coronavirus disease 2019 (COVID-19) is still unclear. Recent reports evidence that, after SARS-CoV-2 infection, male reproductive function and semen quality may be damaged.

**Aim:** To evaluate the semen parameters and inflammation of sexually active men following recovery from SARS-CoV-2 infection at 1 month and 3 months follow-up after the second negative nasopharyngeal swab.

**Materials and methods:** A prospective cross-sectional study on sexually active men recovered from SARS-CoV-2 infection was performed.

For previously hospitalized COVID-19 patients, data on serum inflammatory markers were retrospectively collected.

One month after the second SARS-CoV-2 negative nasopharyngeal swab and 3 months later, four biological fluid samples, namely saliva, pre-ejaculation urine, semen, and post-ejaculation urine, were collected. The occurrence of SARS-CoV-2 RNA in the specimen was evaluated in all the biological fluids collected by RT-PCR. Female partners were retested if any specimen was found to be SARS-CoV-2 positive.

Semen parameters were evaluated according to the World Health Organization manual edition V. Furthermore, semen inflammation was

assessed by quantification of semen leukocytes and interleukin-8 (IL-8) levels and evaluation of a panel of sperm cytokine levels by a two-step ELISA method.

**Results:** A total of 43 men were enrolled in the study. Three patients (7%) tested positive for at least one sample (one saliva; one pre-ejaculation urine; one semen and one post-ejaculation urine), so the next day new nasopharyngeal swabs were collected. The results from these 3 patients and their partners were all negative for SARS-CoV-2.

At 1-month follow-up, 25% of the men with recent SARS-CoV-2 infections and proven healing were oligo-cryptozoospermic, despite the absence of virus RNA in semen. Of the 11 men with semen impairment, 8 were azoospermic and 3 were oligospermic.

Serum inflammatory markers (procalcitonin and C-reactive protein) were analyzed in previously hospitalized patients both at admission and at peak of infection. Levels at admission were statistically significantly higher in patients resulting in crypto-azoospermic with respect to those resulting in normozoospermic ( $p = 0.05$ ;  $p = 0.03$  and  $p = 0.02$ , respectively) after healing.

Oligo-crypto-azoospermia was significantly related to COVID-19 severity ( $P < 0.001$ ).

A total of 33 patients (76.7%) showed pathological levels of IL-8 in semen.

Interleukin-1 $\beta$  and tumor necrosis factor- $\alpha$  levels were significantly negatively related to sperm total number and concentration, whereas interleukin-4 was correlated with sperm motility.

At 3-months follow-up, 8/10 men with semen impairment showed an overall increase of semen parameters compared to levels assessed after 1 month. Of the 4 crypto-/azoo-spermic men 1 month after healing, 2 resulted oligozoospermic, 1 normozoospermic and only 1 remained azoospermic. Two of the 3 oligozoospermic men turned normozoospermic. Semen cytokine levels remained elevated after 3 months, except for IL-6.

**Discussion and conclusion:** SARS-CoV-2 can be detected in saliva, urine, and semen in a small percentage of men who recovered from COVID-19. 25% of men who recovered from COVID-19 demonstrated oligo-crypto-azoospermia. Negative correlations between interleukin-1 $\beta$  and tumor necrosis factor- $\alpha$  and sperm number and the overall high levels of semen cytokines indicate a potential detrimental role of SARS-CoV-2 driven inflammation on spermatogenesis.

An overall tendency to an improvement of semen parameters was found although a genital tract inflammatory condition appears to persist at least 3 months after COVID-19 recovery.

Despite the low number of enrolled patients may limit the statistical power of study and the fact that the previous semen quality of these men was unknown, our results indicate that male of reproductive age recovering from COVID-19 deserve accurate follow-up for their fertility status.