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O-017 mRNA and viral vector COVID-19 vaccines do not affect male fertility

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Study question: Do mRNA and viral vector coronavirus disease 2019 (COVID-19) vaccines detrimentally affect semen parameters?

Summary answer: The semen parameters following COVID-19 vaccination did not reflect any causative detrimental effect from vaccination.

What is known already: Based on a still debatable observation of detrimental effect of COVID-19 infection on male fertility, unfounded claims in the social media suggested a potential association between COVID-19 vaccine and male infertility. To date, only two reports on the possible effect of COVID-19 mRNA vaccines on semen quality are available. First, a study on semen samples from 75 fertile men analyzed only 1–2 months after vaccination concluded that semen parameters following vaccine were predominantly within the normal WHO reference ranges. Secondly, in 45 men comparison of semen before and after COVID-19 mRNA vaccine showed no significant decreases in any sperm parameter.

Study design, size, duration: This prospective study performed at a tertiary public fertility center included 101 men undergoing ART from January 2018 and December 2021. For each man we compared semen parameters before and after the COVID-19 vaccination: 78% of men received mRNA vaccines (78% Pfizer, 22% Moderna), 20% viral vector vaccines (70% AstraZeneca, 30% Johnson & Johnson), and 2% a mixed formulation. Post-vaccine samples were obtained at a median of 2.3 + 1.5 months after the second dose.

Participants/materials, setting, methods: Semen analysis was performed according to WHO guidelines. Medians and interquartile ranges (IQRs) were reported for all parameters. The impact of COVID-19 vaccine on endpoints (semen volume, concentration, motility) was evaluated by Wilcoxon rank sum test to perform paired comparison of pre- and post-vaccination semen parameters. We also evaluated the following covariates: age, BMI, smoke habit, days of sexual abstinence, and frequency of ejaculations. Analyses were carried out by MedCalc[®] software.

Main results and the role of chance: Pre-vaccination samples were obtained after a median abstinence period of 4 days (IQR 3–5) and post-vaccination samples after a median of 3 days (IQR 3–4, $p=0.004$). Pre-vaccination median sample volume, sperm concentration, progressive motility, and total motile sperm count (TMSC) were 3.0 ml (IQR 2.2–4.0), 25.0 million/ml (IQR 11.4–38.0), 50% (IQR 40–60) and 34.8 million (IQR 11.6–68.8), respectively. After the second vaccine dose, the median sample volume significantly decreased to 2.6 ml (IQR 1.9–3.5, $p=0.036$), whereas the median sperm concentration, the progressive motility, and TMSC significantly increased to 43.0 million/ml (IQR 17.0–86.5, $p<0.0001$), 56% (IQR 40–65, $p=0.022$) and 54.6 million (IQR 18.9–105.6, $p<0.0001$), respectively. Thirty-four patients were oligospermic before the vaccine (mean concentration 7.8 + 4.3 million/ml), and also in this subset of patients we observed a significant increase of the median sperm concentration, progressive motility, and TMSC ($p=0.001$, $p=0.002$, $p=0.001$, respectively) in post-vaccine semen samples respect to the pre-vaccine ones. Finally, we analyzed separately patients who received a mRNA vaccine and those who received a viral vector vaccine, and we confirmed the aforementioned results again in these two groups.

Limitations, reasons for caution: Small sample size, short follow-up, no healthy control group, no evaluation of male reproductive potential *i.e.*, by comparing outcomes of ART cycles before and after vaccination. Nevertheless, this work was preceded by only two other reports published on this issue, and it includes more than twice as many patients enlisted.

Wider implications of the findings: In agreement with literature, COVID-19 vaccination does not reduce sperm quality and for the first time we demonstrated that this applies to both mRNA and viral-vector vaccines. The known individual variation in semen and the reduced abstinence time before the post-vaccine sample collection may explain the increases in sperm parameters.

Trial registration number: not applicable