

Effect of SARS-CoV-2 on semen parameters: A meta-analysis of 39 articles from 15 countries

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ADMINISTRATIVE INFORMATION**Support** - N/A.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202420083**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 February 2024 and was last updated on 20 February 2024.**INTRODUCTION**

Review question / Objective The present meta-analysis assessed the effects of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on semen parameters.

Condition being studied The condition being studied is Coronavirus Disease 2019 (COVID-19), a global pandemic caused by the highly contagious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 presents with symptoms such as fever, cough, myalgia, and fatigue, and severe cases can lead to pneumonia or acute respiratory distress syndrome. Some viruses, including SARS-CoV-2, have been associated with adverse effects on male reproductive function, with reports of altered sexual activity and genital symptoms. Studies on semen parameters in

COVID-19 patients have yielded conflicting results, necessitating a meta-analysis to provide more reliable evidence for clinical practice, considering the limitations in existing studies.

METHODS

Search strategy PubMed, Embase, Web of Science, MedRxiv, BioRxiv, and World Health Organization Global Coronavirus databases were searched online for articles published between 1 January 2020 and 25 July 2023. Search terms included sperm, semen, seminal fluid, spermatozoa, fertility, infertility, COVID-19, Coronavirus Disease 2019, SARS-CoV-2, SARS Coronavirus 2, 2019-nCoV, and 2019 Novel Coronavirus.

Participant or population The case group comprises individuals who have undergone follow-

up after SARS-CoV-2 infection, encompassing various demographics such as age, sex, race, vaccination history, and variations in medication during treatment. In contrast, the control group includes individuals who have not been infected with SARS-CoV-2, serving as the reference for comparative analysis of semen parameters.

Intervention SARS-CoV-2 infection or not.

Comparator COVID-19 patients vs. health control.

Study designs to be included Only original research articles were included in this meta-analysis. Studies employing various designs, such as cross-sectional, cohort, or case-control, were considered.

Eligibility criteria Articles were considered eligible if they specifically investigated the impact of SARS-CoV-2 on semen parameters. Included articles were required to provide sufficient data on semen parameters, including but not limited to those associated with sperm volume, concentration, motility, or morphology. No restrictions were placed on the publication status of the articles. Single-arm studies or studies that only provided data on semen parameters at different follow-up time points after SARS-CoV-2 infection were excluded. Studies with incomplete data, such as continuous variables in which only the sample size, median, and interquartile range were provided were also excluded. For repeatedly published articles by the same author, those with a smaller sample size were excluded. Articles that were review papers, meta-analyses, or case reports were excluded. Any studies conducted on animals rather than human subjects were also excluded from consideration.

Information sources PubMed, Embase, Web of Science, MedRxiv, BioRxiv, and World Health Organization Global Coronavirus databases were searched online for articles published between 1 January 2020 and 25 July 2023. For information that is necessary but not shown, contact the corresponding author for enquiry.

Main outcome(s) Sperm volume; Sperm concentration; Total sperm count; Motile sperm count; Progressively Motile sperm count; Sperm vitality; Sperm motility; Progressive sperm motility; Non-progressive sperm motility; Sperm immotility; Normal sperm morphology; Abnormal sperm morphology; Sperm head abnormal; Sperm neck abnormal; Sperm tail abnormal; pH; DNA fragmentation index; Oligospermia; Asthenospermia; Teratospermia; WBC found.

Quality assessment / Risk of bias analysis

Quality of the articles was assessed using the Newcastle-Ottawa Scale, and original articles of poor quality were excluded from the meta-analysis.

Strategy of data synthesis When the heterogeneity test showed $P > 0.05$, the heterogeneity between studies was regarded as insignificant, and a meta-analysis was performed using a fixed-effects model. When the heterogeneity test showed $P < 0.05$, heterogeneity between studies was regarded as significant; meta-analysis was performed using a random-effects model, and subgroup analysis was considered further. However, fixed-effects models were always used when fewer than five studies were included in a certain meta-analysis. Continuous and dichotomous variables were characterised by the mean difference (MD) and odds ratio (OR), respectively. $P < 0.05$ for the combined results of meta-analysis suggests statistical significance. When the number of included studies for a certain parameter was less than three, a meta-analysis was not performed.

Subgroup analysis Subgroup analysis was carried out based on the severity (Mild; Moderate; Severe; Combined/Unclear), follow-up status (Short-term follow-up; Long-term follow-up; Combined/Unclear) and country (China; Iran; Turkey)..

Sensitivity analysis A sensitivity analysis was performed using a one-by-one exclusion method.

Language restriction English.

Country(ies) involved China.

Keywords SARS-CoV-2; COVID-19; semen; sperm; meta-analysis.

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