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The impact of SARS-CoV-2 vaccine on female fertility: a systematic review and meta-analysis

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ABSTRACT

Objective. Most social media users express their fears about vaccine safety as it is believed that SARS-CoV-2 vaccination may affect female reproductive health. The objective of this systematic review and meta-analysis is to evaluate whether WHO-approved SARS-CoV-2 vaccines can affect female fertility.
Materials and Methods. PubMed, ClinicalTrials.gov, the Cochrane Library, and Google Scholar were systematically searched.
Results. In total, 7 clinical trials were included in systematic review and 6 were included in meta-analysis. Studies evaluated the impact of SARS-CoV-2 vaccine on female fertility. In the first meta-analysis, four studies were included and compared the antral follicle count between the vaccinated and unvaccinated groups: MD = 0.12, 95% confidence interval (CI) 0.76-1.01, p = 0.78. The second meta-analysis of two studies compared the AMH level between two groups: MD = 0.18, 95%CI 0.21-0.57, p = 0.37. The third meta-analysis of three studies compared the number of oocytes between the vaccinated and unvaccinated group: MD = 0.32, 95%CI 1.36-0.72, p = 0.55. The fourth meta-analysis of three studies compared the clinical pregnancy rate: RR = 0.89, 95%CI 0.76-1.03, p = 0.13.
Conclusions. Based on our systematic review and meta-analysis regarding fertility rates in vaccinated against SARS-CoV-2 women and unvaccinated ones, we can conclude that there is no statistically significant difference in these two groups in terms of antral follicle count, AMH level, number of retrieved oocytes and clinical pregnancy rates.

INTRODUCTION

The World Health Organization (WHO) declared on 11 March 2020 that the global health emergency caused by SARS-CoV-2 had officially become a pandemic, the first in history to be caused by a coronavirus [1, 2].
As soon as more information on the pathogenesis of SARS-CoV-2 was provided, medical communities around the world, under WHO guidance, im-

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mediately began to develop prophylactic strategies to stop the spread of this virus [3].
As of June 3, 2022, there is a list of 11 WHO-approved vaccines that are accepted and have been successfully used in many countries around the globe [4, 5]. These vaccines demonstrate diverse mechanisms of action, such as mRNA-based vaccines, which play a role of a matrix for viral protein synthesis (Spikevax – Moderna [6]; Comirnaty – Pfizer/BioNTech [7]), vaccines with non-replicating viral vectors containing specific sequences that encode viral proteins (Ad26. COV2.S – Johnson & Johnson [8]; Vaxzevria – Oxford/AstraZeneca [9]), vaccines with viral protein subunits, vaccines with inactivated SARS-CoV-2 (Covilo – Sinopharm [10]), live-attenuated vaccines, *etc*.
Regarding male fertility, according to the World Health Organization, more than 100 million married couples face the problem of infertility, with 40% of cases due to male infertility. Infectious diseases account for 15% of cases of male fertility [11]. Mild SARS-CoV-2 infection is not associated with impaired testes and epididymis function, while patients with moderate SARS-CoV-2 infection have changes in semen parameters: decreased sperm concentration, decreased total number of sperm in the ejaculate, and decreased sperm motility [12-14]. The effect of SARS-CoV-2 on pregnancy and neonatal outcomes is being actively studied, which is why the issues of prevention and its effect on fertility are so relevant [15].
Despite such advances in SARS-CoV-2 prophylaxis, vaccines were believed to be understudied, and people were not eager to vaccinate [16-18]. This hesitancy regarding vaccination once was the most disputable topic on various social media platforms, and in several cases still is [19, 20].
Many social media users are wondering if vaccination affects women's reproductive health, causing menstrual disturbances, infertility, miscarriages, and preterm labour and emotional impact on couples undergoing fertility treatment procedures are prone to developing feelings of psychological distress caused by their infertility diagnosis [21-24]. Probably, the issue could have been provoked in social media due to several studies released in the beginning of pandemic.
Thus, this systematic review and meta-analysis of randomized clinical trials and cohort studies aims to evaluate if WHO-approved SARS-CoV-2 vaccines can affect female fertility.

MATERIALS AND METHODS

The present systematic review was registered in the PROSPERO international prospective registry of systematic reviews by the National Institute of Health Research (NIHR). Protocol and registration number: PROSPERO 2022 CRD42022307531 [25].
Our systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines for reporting systematic reviews [26]. Institutional review board (IRB) approval was not requested since the present study is a review.
Randomized and non randomized clinical trials, case reports, and preclinical studies were included. Papers in other languages than English and studies published only in abstract form were excluded.
An electronic database search was conducted using PubMed, The Cochrane Library, ClinicalTrials.gov, Scopus, Embase and Google Scholar. Authors used a combination of the following terms: "COVID-19", "vaccine", "menstruation", "AMH", "fertility", "ovarian reserve". The date of the last screening was June 1, 2022.
To verify all possibly relevant studies, no restrictions or search filters (publication status, type of article, or language of publication) were applied to the search.
The search strategy in the electronic database PubMed was the following. Using the advanced search builder on PubMed, the following combination of terms was carried out: ((COVID-19) AND (vaccine)) AND (fertility).
The search strategy in electronic databases The Cochrane Library, Scopus and Google Scholar was conducted using the following search terms: COVID-19 AND vaccine AND fertility.
The search was also conducted in the ClinicalTrials. gov electronic database using an advanced search combination: ovarian reserve OR pregnancy OR AMH OR fertility | COVID-19 vaccine.
Additionally, the search was conducted, using MeSH-terms in PubMed ("COVID-19 Vaccines"[Mesh]) AND "Fertility"[Mesh]) and in The Cochrane Library (MeSH descriptor: [COVID-19 Vaccines] explode all trees) and (MeSH descriptor: [Fertility] explode all trees).
The search was conducted independently by four investigators (J.A., E.K., K.M., L.O.) The search results were saved into a reference manager (Zotero, version 6.0.8). All articles were re-checked based on their titles and abstracts following the search. All

types of studies were selected, and each potentially relevant study was obtained in full text and assessed for inclusion independently by the authors. Additionally, a manual search of the references of the retrieved articles was carried out to identify additional studies of interest. Any disagreements regarding the inclusion or exclusion of preselected studies and any other disagreements during the review process were resolved with the help of the fifth author (L.P.).

The primary analysis aimed to evaluate the length of the menstrual cycle, the level of AMH, the antral follicle count. Secondary analysis evaluated clinical pregnancy rates and live birth rates.

The following components were our PICO criteria: "Population" – women of reproductive age, "Intervention" – vaccination against the new infection (with the WHO-approved vaccine), "Comparator" – unvaccinated women, "Outcomes" – menstrual cycle, the level of AMH, the antral follicle count, clinical pregnancy rates and live birth rates.

A risk of bias assessment was performed for each of the included studies using the Cochrane Handbook for systematic reviews of interventions [27]. Five review authors independently assessed the quality of the selected studies. Any disagreements between the reviewers were resolved by discussion with a sixth reviewer (L.P.). Following the Cochrane Handbook for Systematic Reviews of Interventions, the RoB 2 tool [28] was used to assess the risk of bias in randomized controlled studies and ROBINS-I [29] was used for non-randomized studies. According to the Cochrane Handbook for Systematic Reviews of Interventions, an I^2 value of 0 indicates no observed heterogeneity, whereas I^2 values from 30 to 60% may represent moderate heterogeneity, I^2 values from 50% to 90% may represent substantial heterogeneity and I^2 values from 75% to 100% represent considerable heterogeneity.

In addition, these tools were also used to assess the risk of bias arising from reporting biases due to missing results in synthesis. Quality of evidence (QoE) was assessed according to the GRADE system [30]. As for the quantitative synthesis, the meta-analysis was performed using RevMan 5.4 fixed affect model (recommended by the Cochrane Society).

RESULTS

The whole search strategy with the results is presented in the flow diagram (**Figure 1**). We used an electronic search of PubMed, Scopus, Google Scholar, Clinical Trials, and the Cochrane Library

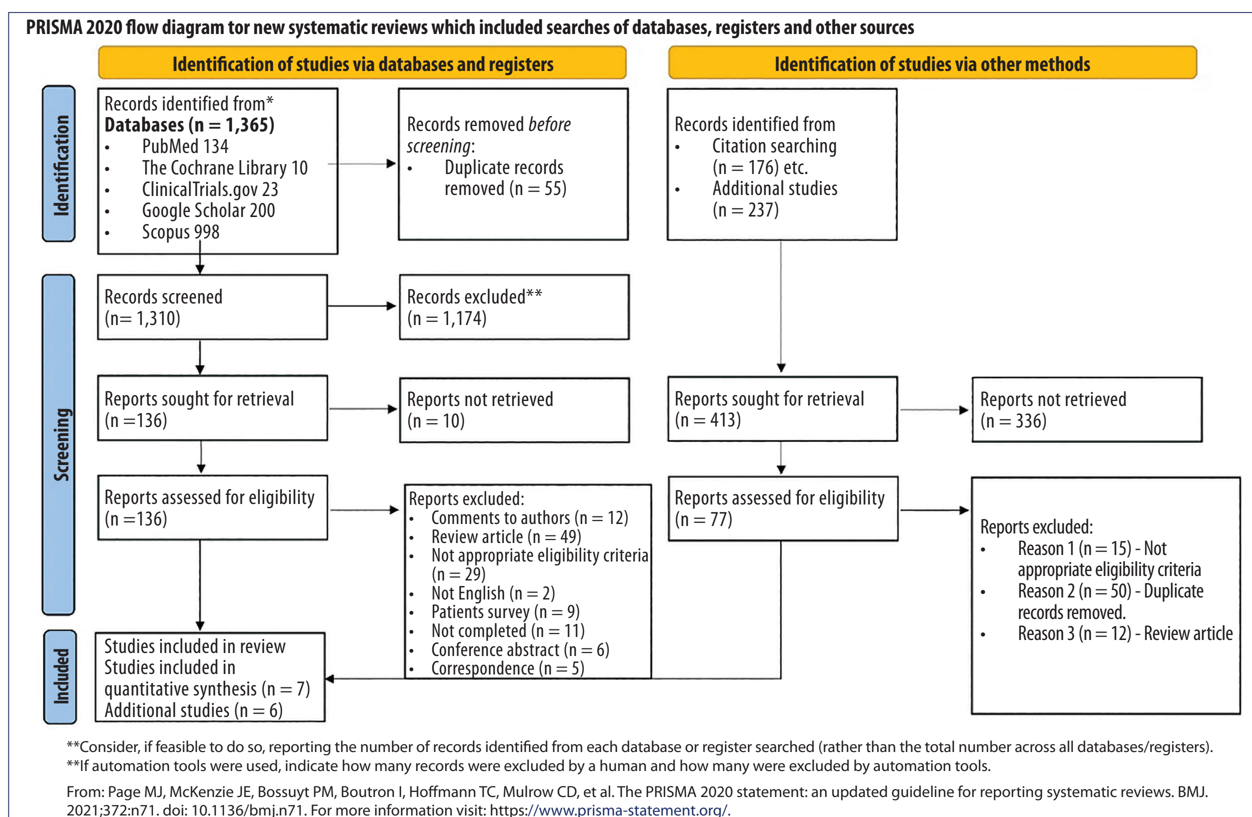

Figure 1. *PRISMA flow chart.*

databases and received 1,365 articles. After removing duplicates and searching for the title and abstract of the articles, 136 publications were selected. Of these, 123 articles were excluded after reading the full texts, 12 studies were comments to the authors, 49 were reviews, two were not in English, 9 were patient surveys, 6 were conference abstracts, 5 were correspondence, and 11 were not completed. Also, due to the absence of relevant inclusion criteria, 29 studies were excluded. Furthermore, we checked the references of the selected articles for acceptable studies (n = 413).

Table 1. *Description of articles included in the systematic review.*

	Study (first author)	Study design	Participants	Interventions	Comparison	Outcomes
1	Soysal *et al.*, 2022 [31]	A prospective cross-sectional study	60 women who applied to the outpatient gynecology clinic	30 vaccinated women mRNA-COVID-19 vaccine (BNT162b2-Pfizer COVID-19 vaccine)	30 unvaccinated women	AMH (4.13 ± 1.94 vs 4.14 ± 2.79; p > 0.05)
2	Odeh-natour, 2022 [32]	A prospective, observational cohort study	59 women undergoing IVF/ICSI cycles	37 vaccinated women two doses of the Pfizer-BioNTech vaccine.	18 unvaccinated women	Number of retrieved oocytes retrieved (10.05 ± 7.6 vs 11.89 ± 9.67; p = 0.63) CPR (44% vs 50%; p = 0.87)
3	Bentov, 2021 [33]	A cohort study	32 women undergoing IVF	9 vaccinated women	14 unvaccinated women	AFC (13.3 ± 4.7 vs 15.6 ± 6.7; p = 0.592) Number of oocytes retrieved (12.4 ± 8.7 vs 11.2 ± 6.7; p = 0.877)
4	Aharon, 2022 [34]	A retrospective cohort study	1205 patients who underwent controlled OHS or single euploid frozen thawed ET	OHS 222 vaccinated women with Pfizer (n = 119) or Moderna (n = 103) vaccine frozen-thawed ET 214 vaccinated women	OHS983 in the control group frozen-thawed ET733 in the control group	OHS AMH (2.9 ± 2.9 vs 2.7 ± 2.6; p = 0.38) AFC (14.9 ± 10.1 vs 13.9 ± 8.5; p = 0.33) No. of eggs retrieved (15.9 [14.4-17.5] vs 15.0 [14.4-15.6]; p = 0.64) frozen-thawed ET AMH (3.3 ± 2.9 vs 3.3 ± 3.0; p = 0.83) AFC (14.4 ± 9.4 vs 13.9 ± 9.7; p = 0.54) CPR (59.5% [52.7-66.3] vs 63.7% [60.2-67.3]; p = 0.27)
5	Huang, 2022 [35]	A retrospective cohort study	2185 patients undergoing fresh IVF cycles	146 vaccinated women 2 dosages of inactivated SARS-CoV-2 vaccines (Sinopharm or Sinovac)	584 unvaccinated women	Number of oocytes retrieved (9.9 ± 7.1 vs 9.9 ± 6.7; p = 0.893) AFC (11.7 ± 6.8 vs 11.9 ± 6.9; p = 0.764) CPR n/N (%) (39/66 (59.1) vs 150/236 (63.6); p = 0.507)
6	Avraham, 2022 [36]	A retrospective cohort study.	400 patients who underwent IVF	200 vaccinated women 2 doses of the BNT162b2 (Pfizer-BioNTech) 128 patients who underwent ET cycles. 66 patients who underwent freeze-all ET cycles.	200 unvaccinated patients 133 patients in the ET cycles group. 47 patients in the freeze-all ET group.	Number of oocytes retrieved (10.63 [9.82-11.43] vs 10.72 [9.53-11.91]; p = 0.93) ET Number of oocytes retrieved (8.47 [7.52-9.42] vs 8.32 [7.38-9.27]; p = 0.78) CPR n/N (%) (42/128 (32.8) vs 44/133 (33.1); p = 0.96) freeze-all ET Number of oocytes retrieved (14.88 [12.07-17.69] vs 13.62 [10.89-16.34]; p = 0.95)
7	Jacobs, 2022 [37]	A retrospective cohort study	280 patients undergoing IVF-fresh ET cycles	142 vaccinated women mRNA-1273 (Moderna) - 70 BNT162b2 (Pfizer-BioNTech) - 65 Ad26.COV2.S (Janssen) - 7	138 nonvaccinated women	AFC (23 ± 13 vs 24 ± 15) Number of oocytes retrieved (14 ± 8 vs 15 ± 9); p = 0.33) CPR n/N (%) (65/142 (45.8) vs 74/138 (53.6))

We selected 77 articles for full text review, but 50 of them were duplicates, 12 studies were review articles, and 15 publications were excluded due to non-compliance with our criteria. Therefore, a total of seven studies were included in the final analysis, which yielded a total of 3,700 patients (**Table 1**). All 7 studies were non randomized. **Table 2** presents the list of studies with other study designs (prospective studies, case reports, observational studies). **Table 3** presents the list of excluded studies with reasons. According to the Cochrane Handbook, four reviewers (E.K., L.O., K.M.) assessed the risk of bias of each included study. Each element was classified as critical, serious, or low risk of bias in the ROBINS-I tool for non randomized trials. Any disagreements were resolved by discussion with other authors (L.P., J.A.).

Table 2. *The list of additional studies.*

Study (first author)	Type of study	Participants/population	Outcome(s)
Wesselink *et al.* (2022) [38]	An internet-based, prospective, preconception cohort study	Participants who enrolled between December 14, 2020, and September 22, 2021 (*n* = 2,679)	Female participants who received at least 1 dose of vaccine before a given menstrual cycle had 1.08 times the probability of conceiving during that cycle compared with unvaccinated participants (95%CI 0.95-1.23)
Edelman *et al.* (2022) [39]	Prospective study	3,959 individuals (vaccinated 2,403; unvaccinated 1,556)	COVID-19 vaccine was associated with a less than 1-day change in cycle length for both vaccine-dose cycles compared with pre-vaccine cycles (first dose 0.71 day-increase, 98.75%CI 0.47-0.94; second dose 0.91, 98.75%CI 0.63-1.19); unvaccinated individuals saw no significant change compared with three baseline cycles (cycle four 0.07, 98.75%CI -0.22-0.35; cycle five 0.12, 98.75%CI -0.15-0.39). In adjusted models, the difference in change in cycle length between the vaccinated and unvaccinated cohorts was less than 1 day for both doses (difference in change: first dose 0.64 days, 98.75%CI 0.27-1.01; second dose 0.79 days, 98.75%CI 0.40-1.18). Change in menses length was not associated with vaccination.
Kolatorova *et al.* (2022) [40]	Case series	36 women	FSH (IU/L) • Before the 3rd Dose of COVID-19 Vaccine: 6.2 (5.8, 8.6) • After the 3rd Dose of COVID-19 Vaccine: 6.49 (5.045, 8.660) AMH (ng/mL) • Before the 3rd Dose of COVID-19 Vaccine: 3.25 (1.46, 5.09) • After the 3rd Dose of COVID-19 Vaccine: 3.03 (1.68, 5.04) AFC • Before the 3rd Dose of COVID-19 Vaccine: 23 (19.5, 28.75) • After the 3rd Dose of COVID-19 Vaccine: 24 (21.50, 28.75) Menstrual cycle changes • After the first and second vaccine doses, 92% of women did not observe changes in their cycle. After the third dose, the percentage of women reporting no cycle changes decreased to 64%, while 20% of woman reported cycle prolongation, 8% cycle shortening and 4% bleeding out of cycle.
Orvieto *et al.* (2021) [41]	An observational study	36 couples	No influence of mRNA SARS-CoV-2 vaccine on patients' performance during their immediate subsequent IVF cycle, reflecting no detrimental effects of the vaccine on patients' ovarian reserve, nor the developing gametes/embryos, with an acceptable pregnancy rate (30% per transfer).
Mohr- Sasson *et al.* (2022) [43]	Prospective study	129 women	Menstruation length (days) • < 30 years: 4.6 ± 1.2 • 30-35 years: 5.2 ± 1.6 • > 35 years: 4.6 ± 1.5 Change (%) in AMH • < 30 years: -1.6 ± 28.6 • 30-35 years: -10.8 ± 43.9 • > 35 years: 5.8 ± 61.5
Horowitz (2022) [44]	Prospective study	31 women	The median AMH concentrations before and after COVID-19 vaccine were comparable (1.7 *versus* 1.6 g/ml, respectively, p = 0.96). No correlation was found between the participant's anti-COVID-19 antibody titre and the change in AMH concentration.

Table 3. *The list of excluded studies.*

Studies	Reasons for exclusion
Ripabelli *et al.* 2021 [45]	None of our outcomes was reported.
Mattar *et al.* 2021 [46]	Evaluates whether mRNA enters breast milk.
Castiglione Morelli *et al.* 2022 [46]	Women who received vaccination against SARS-CoV-2 infection and recovered COVID-19 patients.
Goldshtein *et al.* 2021 [48]	The association between the receipt of the mRNA vaccine and the risk of SARS-CoV-2 infection among pregnant women.
Edelman *et al.* 2022 [49]	None of our outcomes was reported.
Fell *et al.* 2022 [50)	The impact of the COVID-19 vaccine on pregnancy.
Magnus *et al.* 2022 [51]	The impact of the COVID-19 vaccine on pregnancy.
Abdollahi *et al.* 2022 [52]	None of our outcomes was reported.
Golan *et al.* 2021 [53]	The impact of the COVID-19 vaccine on pregnancy.
Magnus *et al.* 2021 [54]	The impact of the COVID-19 vaccine on pregnancy.
Rottenstreich *et al.* 2021 [55]	The impact of the COVID-19 vaccine on pregnancy.
Bleicher *et al.* 2021 [56]	The impact of the COVID-19 vaccine on pregnancy.
Dagan *et al.* 2021 [57]	The impact of the COVID-19 vaccine on pregnancy.
Setti *et al.* 2021 [58]	The impact of the COVID-19 vaccine on pregnancy.
Richardson *et al.* 2022 [59]	The impact of the COVID-19 vaccine on pregnancy.
Lu-Culligan *et al.* 2022 [60]	Impact of COVID-19 on animals.
Moro *et al.* 2022 [61]	The impact of the COVID-19 vaccine on pregnancy.
Wainstock *et al.* 2021 [62]	The impact of the COVID-19 vaccine on pregnancy.
Stock 2022 [63]	The impact of the COVID-19 vaccine on pregnancy.
Bookstein Peretz 2021 [64]	The impact of the COVID-19 vaccine on pregnancy.
Brock Aleisha *et al.* 2021 [65]	None of our outcomes was reported.
Skjefte *et al.* 2021 [66]	The impact of the COVID-19 vaccine on pregnancy.
Alvergne *et al.* 2021 [67]	None of our outcomes was reported.
Liperis *et al.* 2022 [68]	Published only in abstract form.
Sengupta *et al.* 2022 [69]	None of our outcomes was reported.
Chung *et al.* 2021 [70]	Survey about vaccination.
Samannodi 2021 [71]	Survey about vaccination.
Sutton *et al.* 2021 [72]	Survey about vaccination.

The visualization tools were created by the ROB-VIS app. This app created "‹traffic light" graphs of the domain-level judgements for each result and weighted bar graphs of the distribution of risk of bias judgments within each bias domain. The overall risk of bias for the non randomized trials was moderate, according to the ROBINS-I tool (**Figure 2**). The QoE was moderate due to methodological diversity (**Table 4**). The primary analysis focused on dynamic variations of serum AMH levels (1.2 ng/ml and higher), antral follicle count (the number of follicles measuring 2-10 mm in size from both ovaries), and the number of oocytes retrieved. The secondary analysis evaluated clinical pregnancy rates. We have conducted four meta-analyses with different comparisons to avoid biases.

In the first meta-analysis, four studies were included and compared the antral follicle count between the vaccinated and unvaccinated groups: MD = 0.12, 95%CI 0.76-1.01, p = 0.88. The heterogeneity for this comparison was 6%. There was no significant difference between the two groups (**Figure 3A**). There were no differences in antral follicle count for the vaccinated group *vs* unvaccinated group.

The second meta-analysis of two studies compared the level of AMH between two groups: MD = 0.18, 95%CI 0.21-0.57, p = 0.37. The heterogeneity for this comparison was 0%. Consequently, there was no significant difference between the vaccinated and unvaccinated groups (**Figure 3B**).

The third meta-analysis of four studies compared the number of oocytes between the vaccinated and unvaccinated groups (MD = 0.32, 95%CI 1.36-0.72, p = 0.55). The heterogeneity for this comparison was 0%. Hence, there was no significant difference between the two groups (**Figure 3C**).

The fourth meta-analysis of three studies compared the clinical pregnancy rate between two groups: (RR = 0.89, 95%CI 0.76-1.03, p = 0.13). Consequently, there was no significant difference between the vaccinated and unvaccinated groups (**Figure 3D**). The heterogeneity for this comparison was 0%.

Moreover, supplementation with myo-ins during assisted reproductive technologies reduces the total amount of gonadotropins and leads to improvements in oocyte quality and maturation and embryo development and an increase in the rate of successful pregnancies. In the studies of patients who underwent IVF treatments, ovarian response and pregnancy rates were similar in patients who were vaccinated with the SARS-CoV-2 mRNA vaccine before IVF treatment compared to those of unvaccinated women [42].

Table 4. *Summary of evidences.*

Certainty assessment							No of patients		Effect		Certainty
No of studies	**Study Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Considerations**	**Vaccination against COVID-19**	**No vaccination**	**Relative (95%CI)**	**Absolute (95%CI)**	
Difference between AFC in two groups											
4	Observational studies	Serious[a]	Not serious	Not serious	Not serious	None	519	1719	-	MD 0.12 higher (0.76 lower to 1.01 higher)	⊕⊕⊕◯ Moderate
Difference in AMH level in two groups											
2	Observational studies	Serious[a]	Not serious	Not serious	Not serious	None	252	1013	-	MD 0.18 higher (0.21 lower to 0.57 higher)	⊕⊕⊕◯ Moderate
Number of oocytes retrieved in two groups											
4	Observational studies	Serious[b]	Not serious	Not serious	Not serious	None	334	754	-	MD 0.32 lower (1.36 lower to 0.72 higher)	⊕⊕⊕◯ Moderate
Difference in CPR in two groups											
3	Observational studies	Serious[a]	Not serious	Not serious	Not serious	None	143/336 (42.6%)	268/507 (52.9%)	RR 0.89 (0.76 to 1.03)	58 fewer per 1,000 (from 127 fewer to 16 more)	⊕⊕⊕◯ Moderate

CI: confidence interval; MD: mean difference; RR: risk ratio; amoderate risk of bias in classification of interventions; bmoderate risk of bias in classification of interventions and bias due to missing data.

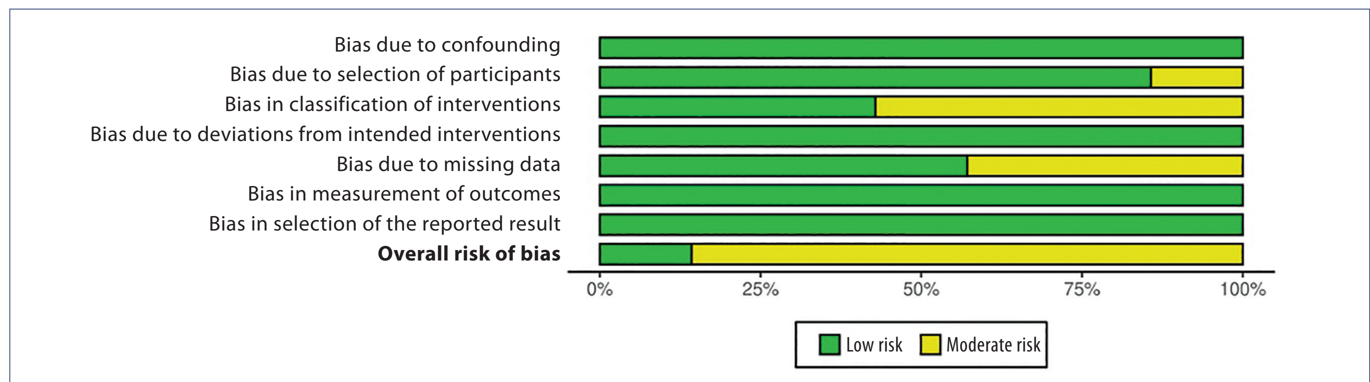

Figure 2. *Risk of bias graph from the included studies.*

The results of a case series by Kolatorova *et al.* [40] showed that after the first and second doses of the vaccine, 92% of women had no changes in the cycle. After the third dose, the percentage of women reporting no change in their cycle dropped to 64%, while 20% of women reported cycle lengthening, 8% cycle shortening, and 4% extra-cycle bleeding. More-Sasson *et al.* [43] in a prospective study did not observe significant differences in the change in the duration of the menstrual cycle before and after vaccination for any of the three groups ($p = 0.281$).

We cannot estimate the length of the menstrual cycle because there were not enough studies to conduct a meta-analysis.

DISCUSSION

The results of our meta-analyses demonstrate the absence of a statistically significant difference in the studied outcomes of fertility rates between two groups (women vaccinated against SARS-CoV-2 and unvaccinated).

Controversies around vaccination against SARS-CoV-2 among women of reproductive age were once created and still pose a serious epidemiological issue with respect to the safety of women. Most social media users express their fears about vaccine safety, with its effect on female reproductive health being one of them. This social media literature actively spreads assumptions

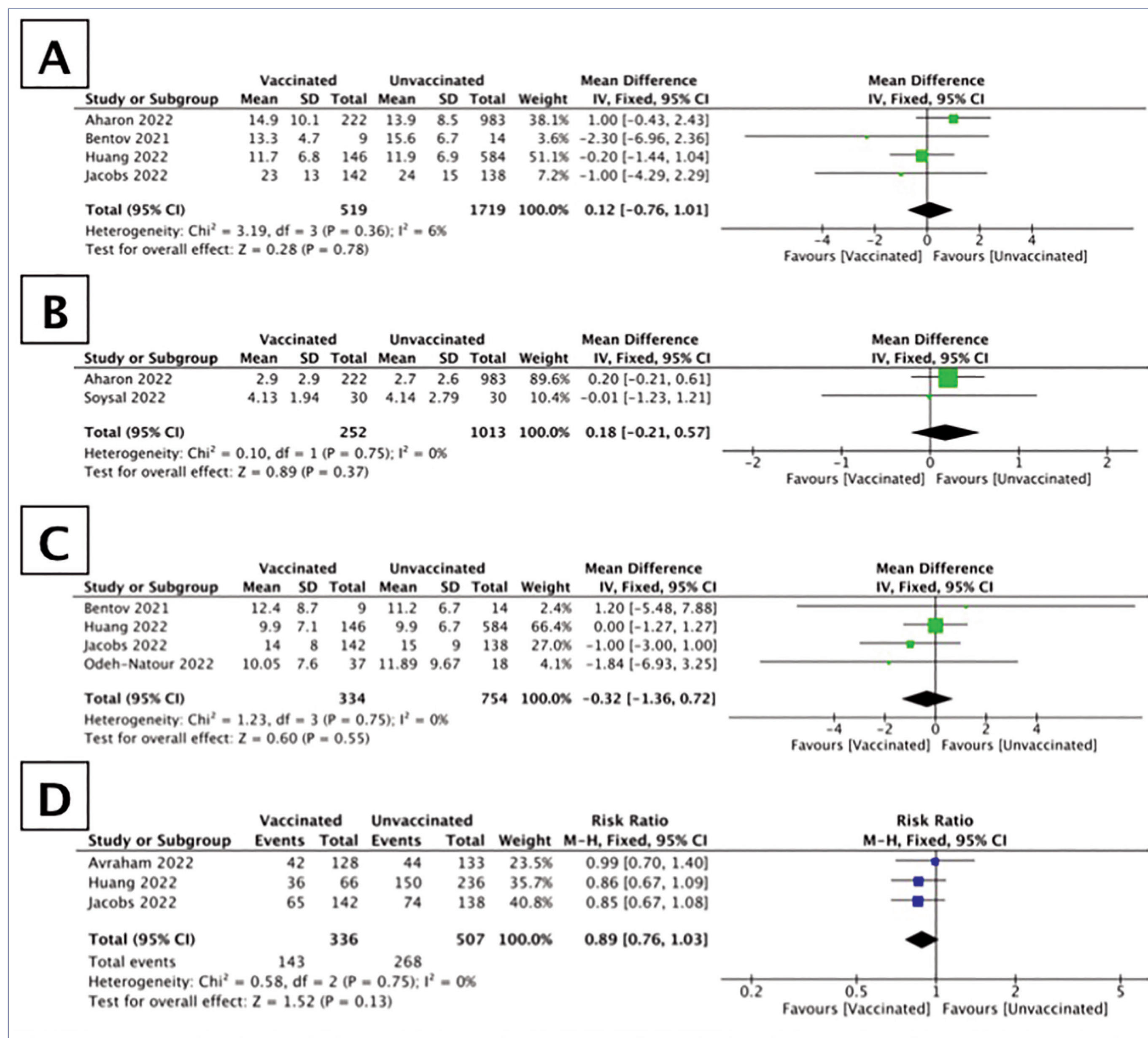

Figure 3. *Forest plots showing the difference* ***(A)*** *between AFC;* ***(B)*** *in AMH level;* ***(C)*** *retrieved oocytes;* ***(D)*** *in CPR two groups.*

that SARS-CoV-2 vaccination can result in infertility, poor outcomes of IVF, menstrual problems in non-pregnant women, preterm labours, and miscarriages in pregnant ones. Gynaecologists around the world are currently collecting evidence against these misconceptions by analysing large databases of women who received the SARS-CoV-2 vaccine.

The European Society of Human Reproduction and Embryology (ESHRE) recommends delaying assisted reproduction treatments (sperm collection, ovarian stimulation, embryo transfer) for at least a few days after the completion of vaccination, *i.e.*, after the second dose. It also mentions vaccination in pregnancy by stating that this question should be discussed with a healthcare professional [73].

Absolutely, counselling women about the benefits and potential side effects of vaccines is crucial. Visconti *et al*. [74] demonstrated that more than half of our study population declared that vaccines during pregnancy are not safe. A crucial role is played by a lack of appropriate counselling and support from consultant's obstetrician. SARS-CoV-2 pandemic has sensitized the entire population about the importance of prevention and vaccination, therefore, health care specialist should take advantage from that and put strong efforts in implementing counselling strategies and vaccine campaigns.

Ensuring women are well-informed empowers them to make informed decisions about their health. This awareness plays a significant role in achieving high compliance with vaccination rec-

ommendations, ultimately contributing to public health efforts [74].

The strengths of our work are associated with adherence to the PRISMA checklist methodology and the Cochrane Handbook for systematic reviews.

When looking for publications for our systematic review, we included many studies that demonstrated no or minimal effect of SARS-CoV-2 vaccines on female reproductive health. Unfortunately, the design of some studies that provided strong evidence did not follow our review protocol due to the long-term results, and we were forced to exclude them.

Despite the favourable results of our review, several limitations can affect these results. Firstly, the WHO defines infertility as the failure to conceive after 12 months or more of regular unprotected sexual intercourse [75]. The evaluation of fertility in women should be performed in a systematic, expeditious, and cost-effective way to identify all relevant factors, with an initial emphasis on the least invasive methods to detect the most common causes of infertility [76]. In this sense, the follow-up period during which fertility assessment needs to be performed should not be less than one year. Second, several studies reveal a decrease in ovarian reserve, a decrease in AMH, and reproductive endocrine disorders in women with a medical history of SARS-CoV-2 infection [77]. In this case, taking into account the fact that some patients willingly avoid doctor visits while having minimal respiratory symptoms or the manifestations of SARS-CoV-2 disease were unremarkable and were not noticed by the patients, we can assume that some patients included in the investigation could have had no documented history of mild SARS-CoV-2 disease and, in fact, could probably have affected the results, as they may have had laboratory and clinical signs of infertility. Finally, although the mechanism of action of various SARS-CoV-2 vaccines differs, some articles do not pay attention to that and include patients in studies without separating them into groups according to the specific type of vaccine they used.

The limitations of our systematic review and meta-analysis were the low quality of some of the included studies and the limited size of the studies. The studies used different vaccines. Another limitation of the studies is the age of the patients, since follicular count and AMH are associated with age. Similarly with the presence of absence of gynaecologic pathology. AMH from study Soysal *et al*. [31] seems to be from a non-infertility outpatient clinic and AMH from Aharon *et al*. [34] is from a population seeking fertility care.

Implications for future research may include involving more patients in the study in order to produce more unbiased results, separating patients into different vaccine groups according to the mechanism of action, since it is prudent to know if there are differences between WHO-proven vaccines. More detailed exploration of sources of heterogeneity and subgroup analyses based on vaccine type, dosage, and participant demographics could provide valuable insights into the observed variability in the findings. Also, the length of the menstrual cycle should be evaluated in studies of better design.

CONCLUSIONS

Based on our systematic review and meta-analysis of fertility rates in women vaccinated against SARS-CoV-2 and unvaccinated, we can conclude that there are no statistically significant differences between these two groups in terms of antral follicle count, AMH level, number of retrieved oocytes, and clinical pregnancy rates. Furthermore, seven well-conducted clinical trials were included to summarize all available data and provide an evidence-based answer to dispel the myth about fertility and vaccination.

COMPLIANCE WITH ETHICAL STANDARDS

Authors' contribution

L.A., L.P.: Conceptualization. L.P., K.M., E.K., J.A.: Data curation, methodology. L.O., J.A., L.P., K.M., E.K.: Writing - review & editing. L.O., J.A., L.P., K.M., E.K., L.A., L.P.: Validation.

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Disclosure of interests

The authors declare that they have no conflict of interests.

Ethical approval

N/A.

Informed consent

N/A.

Data sharing

Data are available along with the review.

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