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**MRNA COVID-19 VACCINES DO NOT COMPROMISE IMPLANTATION OF EUPLOID EMBRYOS**

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**OBJECTIVE:**

Concerns have arisen in the lay press regarding a theoretical impact of the COVID-19 vaccine on fertility and early pregnancy. These concerns originate from speculation regarding homology between the COVID-19 spike protein targeted by the vaccine and syncytin-1 protein, which mediates cytotrophoblast and syncytiotrophoblast fusion and placental development.<sup>1</sup> While this theory has been deconstructed by immunology experts, robust clinical studies have yet to examine a relationship between the mRNA COVID-19 vaccines and reproductive potential. This study aims to assess whether COVID-19 vaccination status impacts early pregnancy outcomes in patients undergoing IVF.

**MATERIALS AND METHODS:**

This study included patients who underwent single euploid frozen-thawed embryo transfer (FET) at a single academic center. Vaccinated patients who received the second dose of the Pfizer or Moderna mRNA vaccine two weeks prior to single euploid FET were compared to non-vaccinated patients who underwent single euploid FET during the same time period. Patients who received vaccine doses less than 14 days prior to FET were excluded. Outcomes included pregnancy rate (HCG  $\geq 2.5$  IU/L), clinical pregnancy rate (presence of a gestational sac on ultrasound), ongoing pregnancy rate, and pregnancy loss rate. Statistical analysis was performed using Chi-square, Student's t-test, and multivariable logistic regression to control for confounders.

**RESULTS:**

Of the 65 patients who underwent single euploid FET two weeks after their final vaccine dose, 28 patients received the Pfizer vaccine and 37 received the Moderna vaccine. Fully vaccinated patients underwent FET between February-April 2021. During that time period 328 non-vaccinated patients underwent single euploid FET and comprised the control group. Baseline characteristics including age, oocyte age, BMI, AMH, BAFC, and endometrial thickness were similar between the groups. Vaccinated and non-vaccinated patients had similar pregnancy rates (75.6% vs. 73.0%,  $p=.72$ ) and clinical pregnancy rates (63.4% vs. 56.9%,  $p=.43$ ). No significant differences were seen in pregnancy loss rates (11.8% vs. 23.2%,  $p=.13$ ) or ongoing pregnancy rates (66.7% vs. 56.1%,  $p=.18$ ) between the groups. Controlling for age, BMI, AMH, and endometrial thickness revealed no association between vaccination and early pregnancy outcomes (Pregnancy: aOR 1.15, 95% CI 0.49-2.75,  $p=.75$ ; Clinical pregnancy: aOR 1.42, 95% CI 0.65-3.10,  $p=.38$ ; Ongoing pregnancy: aOR 1.67, 95% CI 0.77-3.61,  $p=.19$ ; Pregnancy loss: aOR 0.39, 95% CI 0.11-1.37,  $p=.14$ ).

**CONCLUSIONS:**

Administration of COVID-19 mRNA vaccines does not interfere with early pregnancy in patients who undergo transfer of genetically screened embryos. There is no relationship between immune response to the COVID-19 spike protein and placental development.

**IMPACT STATEMENT:**



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Patients who are planning pregnancy can be reassured that COVID-19 vaccination does not adversely impact early pregnancy outcomes. Our findings serve to debunk circulating myths and substantiate that the risk/benefit ratio supports vaccination in women who are trying to conceive.

**REFERENCES:**

1. Male V. Are COVID-19 vaccines safe in pregnancy? *Nat Rev Immunol.* 2021 Apr;21(4):200-201. doi: 10.1038/s41577-021-00525-y. Erratum in: *Nat Rev Immunol.* 2021 Mar 12;; PMID: 33658707; PMCID: PMC7927763.