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Is There any Effect of COVID-19 on Follicular Environment in Women Underwent ART?

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Abstract

There is insufficient data on the impact of severe acute respiratory coronavirus-2 (SARS-CoV-2) on the reproductive tissues, its possible risk of cross-contamination, transmission and adverse effect on in vitro fertilization (IVF) outcome. Until today, there is no report associated with viral RNA in both follicular fluid and embryo culture medium from SARS-COV-2 positive women. In this case report, a 24-year-old woman with SARS-CoV-2 was presented. We investigated the SARS-COV-2 positivity in the follicular fluid and embryo culture medium of mildly symptomatic woman on oocyte pick up (OPU) day. We could not detect viral RNA in neither the follicular fluid nor the embryo culture medium. In addition, although the response of ovarian stimulation was normal, the number and maturity of the retrieved oocytes were low.

Keywords: SARS-COV-2, In vitro fertilization, Oocyte retrieval, Follicular fluid, Embryo culture medium

Introduction

Severe acute respiratory coronavirus-2 (SARS-CoV-2) binding proteins were demonstrated in testis, ovary, endometrial, and placental cells. We firstly investigated the SARS-COV-2 positivity in both follicular fluid and embryo culture medium of mildly symptomatic woman on oocyte pick up (OPU) day.

Case Report

A 24-year-old woman who had been trying to conceive for nearly 5 years without success after gonadotrophin and intrauterine insemination therapy, was treated with in vitro fertilization (IVF) due to unexplained infertility. After a negative polymerase chain reaction (PCR) test result, the ovarian stimulation was started with recombinant follicle-stimulating hormone (FSH) (Gonal-F®; Merck Serono, Bari, Italy) 150 IU/day from the third day of the cycle and GnRH antagonist (Cetrotide®; Merck, Idron France) was added from cycle day 8 when the leading follicle reached a diameter of 12-14 mm. In each visit for follicular monitoring, temperature and symptoms questionnaire checking were performed. On the hCG trigger day, 5 follicles on the right and 4 follicles on the left at least ≥17 mm in diameter were detected. Peak estrogen level was 1480 pg/mL. The ovulation was triggered with recombinant human chorionic gonadotropin (r-hCG) (Ovitrelle®; 250 mcg/0.5 mL, Merck Serono, Modugno, Italy). SARS-CoV-2 PCR test was repeated for both the patient before OPU and her husband before intracytoplasmic sperm injection (ICSI) procedure. After 24 hours, we received two negative PCR test results. On OPU day, she complained of headache and mild nausea. As in all cases including this one, all staff were wearing appropriate personal protective equipment (PPE) including N95 masks, eye shielding glasses and gloves in the operation room. The patient had a surgical mask, too. Transvaginal oocyte retrieval procedure was performed under sedation anesthesia. Although COVID-19 PCR test was negative, embryology team was informed about the symptoms of the patient. Firstly, we picked up oocytes from the right ovary. However, we could not find any oocyte from the right side, unexpectedly. Before the retrieval of the oocytes from the left ovary, serum hCG level was measured from venous blood, immediately. As the result was found as 135 mIU/mL, we continued retrieval of oocytes from left ovary. Four oocytes were picked up, 3 of which of them was M1 and 1 was germinal vesicle. In addition, we studied FSH and luteinizing hormone (LH) receptor gene mutations and they resulted as negative. All follicle samples were separated for SARS-CoV-2 PCR test. We consulted the patient to the Infectious Disease Clinic and hospitalized her to follow up. After OPU procedure, PCR tests repeated twice were again negative. The day after, her headache persisted. After 24-hour incubation, all of the oocytes evaluated as M2 were inseminated with ICSI. PCR test was performed again 24 hours after OPU and the this nasopharyngeal swab PCR test was positive, but we could not detect viral RNA in neither the follicular fluid nor

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the embryo culture medium. Serum C-reactive protein level of the patient was 45 mg/L, neutrophil- lymphocyte ratio was 7. Favipiravir and low molecular weight heparin were started. On the third day, one grade 2 embryo with 8 cells was vitrified in a separate tank. Medical therapy for COVID-19 disease was continued for 2 days in the hospital. Then, her symptoms improved and her PCR test returned to negative. Therefore, she was discharged from the hospital for isolation at home for 14 days. She continued to the favipiravir 600 mg 2×1 for 5 days and low molecular weight heparin 0.4 cc 1×1/day treatment for 10 days at home.

Discussion

In the literature, this is the first report presenting the negative PCR test results for SARS-CoV- 2 virus in both follicular fluid and embryo culture medium from a mildly symptomatic woman with COVID-19.

Rajput et al showed the expression of ACE 2 and TMPRSS2 receptors on oocytes, zygotes, and blastocysts from healthy women for potential entry of SARS-CoV-2 (1). However, whether the virus would attack directly to the oocytes and embryos or indirectly affect them is still unknown. Barragan et al could not detect viral RNA of SARS-CoV-2 in 16 oocytes from two women who were positive on OPU day by PCR (2). Demirel et al did not find viral RNA in the follicular fluid aspirate from a SARS-CoV-2 woman (3). We also could not find viral RNA of SARS-CoV-2 in neither the follicular fluid nor the embryo medium from mildly symptomatic positive woman by PCR. Although the absence of FSH and LH gene receptor mutations and the response of ovarian stimulation was normal, we could not retrieve any mature oocytes, unexpectedly.

Conclusions

Although we did not detect viral RNA of SARS-CoV- 2 in neither the follicular fluid nor the embryo culture medium of a COVID-19 infected woman, the symptom based triage and using of PPE are very important during pandemic. Further studies are needed to clarify the effect of COVID-19 on woman's reproductive systems.

Authors' Contribution

NY, OMT and ZK: concept and design. CO and SA: data collection and interpretation of the data. NY and ZK: performing of the study and writing of the draft. All authors read and approved the study.

Conflict of Interests

Authors declare that they have no conflict of interests.

Ethical Issues

We received ethical approval from the Ministry of Health of Republic of Turkey with a number 2021-04-07T12_38_49.

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