Abstract title: Is COVID-19 symptomatic triage enough? The limited value of serological testing

Study question:
Do serological and molecular tests increase the detection of patients with SAR-CoV-2 after a negative triage?

Summary answer:
Serological testing has limited value in detecting SARS-CoV-2 once triage has been negative if molecular testing is being performed before oocyte retrieval or embryo transfer.

What is known already:
Fertility community is uncertain about how to optimally provide care to infertile patients, without compromising safety, once the activity is re-established. The key principle established by the scientific societies for resuming activity is that anyone attending a clinic should be triaged negative. More precise methodology has been developed such as immunological tests that inform us of the state of the disease and molecular tests (RT-PCR) that measures viral load. These tests may help us to identify asymptomatic and pre-symptomatic carriers that could have not been detected only with triage and patients with past infections that may need no further tests.

Study design, size, duration:
Between April 27th and May 19th, 2020, 1549 women were tested for SARS-CoV-2. Before these tests were performed, a symptomatic triage had been carried out in which patients were asked by telephone for the presence of symptoms of the virus or if they had been in contact with someone suspected or confirmed to have been infected with the disease. Only patients classified as negative triage attended the clinic for further testing.

Participants/materials, setting, methods:
IgG and IgM antibody against SARS-CoV-2 in plasma samples were tested using enzyme linked immunosorbent assay (ELISA) kits (Epitope Diagnostics, USA). Women with asymptomatic triage and negative IgM started a treatment; on the 5th-8th day of stimulation for retrieval or 3-5 days before a
frozen embryo transfer, a nasopharyngeal RT-PCR was performed in order to avoid an active infection during the treatment.

**Main results and the role of chance:**
Study was performed in 17 private clinics belonging to IVIRMA group. Serological testing was carried out in 1549 patients before starting a treatment. Seroconversion rate for IgG was 3.8% (n=59) and for IgM was 0.7% (n=11). As previously discussed, only those patients in whom the recent presence of the infection had been ruled out (IgG+/IgM- or IgG-/IgM-) continued with the treatment. Before embryo transfer, both in fresh and frozen cycles, a molecular determination of the virus was carried out and we observed a 0.06% (n=1) rate of positive RT-PCR.

The possibilities of having a patient with negative IgG and IgM and a positive RT-PCR is due to the period between the pre-symptomatic or asymptomatic shedding and the first time at which the production of IgM starts, which can be up to 12 days. Even though a negative RT-PCR could be considered enough as immunity is not well established, there is no clear evidence that past infections could be re-infected, and IgG seem to be neutralizing. Serological testing of IgM prevents patients from starting endometrial priming or controlled ovarian stimulation decreasing the risk of cancelling the cycle while a positive IgG avoids repeating RT-PCR for each oocyte retrieval or embryo transfer.

**Limitations, reasons for caution:**
The low prevalence of infected patients after the triage makes these number very approximate. The utility of these tests will worsen as the virus incidence decreases.

**Wider implications of the findings:**
In this current scenario, serological testing does not seem to be a cost-effective strategy to avoid asymptomatic carriers of the virus for starting a treatment, but it still detects a low number of asymptomatic patients. Lower occurrence of the virus may suggest the no need for a later screening.

**Keywords:**
SARS-CoV-2
serological testing
triage