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O-192 Concomitant autoimmunity in endometriosis-affected women and In Vitro Fertilization (IVF) outcomes: a cohort study

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Study question: To evaluate whether the presence of concomitant autoimmunity in endometriosis patients may affect In Vitro Fertilization (IVF)/ Intracytoplasmic Injection (ICSI) outcomes.

Summary answer: In 'normo-responders' patients autoimmunity did not affected ovarian response to gonadotrophin stimulation yet was the only significant negative predictor of cumulative pregnancy rate (CPR).

What is known already: In the last years, endometriosis has been redefined as a multifactorial disease with a complex pathogenesis. In this setting, a role of both innate and adaptive immune systems have been proposed in endometriosis development. The coexistence of endometriosis and autoimmunity is well-documented. Also, an increased risk of more severe stages of endometriosis in patients with autoimmunity has been recently reported. Even if autoimmunity has been associated with lower pregnancy rates and higher miscarriage rates, whether the presence of autoimmunity in endometriosis patients could act as an additive factor worsening IVF/ICSI response is still not known.

Study design, size, duration: Single-center, retrospective, cohort study. First IVF/ICSI cycles of endometriosis patients with or without autoimmunity carried out from 2007 to 2021 at the Fertility Unit of IRCSS San Raffaele Hospital(Milan) were included. Patients with endometriosis and concomitant autoimmunity were age-matched to endometriosis only controls. Only patients with a complete disease control following endometriosis treatment were admitted to IVF/ICSI. A total of 471 patients were enrolled. The study was conducted according to STROBE guidelines for observational studies.

Participants/materials, setting, methods: Endometriosis diagnosis was surgical/histopathological, yet also ovarian endometriosis at ultrasound assessment by expert operators was included. Autoimmunity was assessed by blood tests for auto-antibodies and/or rheumatological records. Stratified analysis by "expected" ovarian response at baseline according to AFC and/or AMH were performed. Expected 'poor-responders' were defined according

to Bologna Criteria. The primary outcome was CPR. Secondary outcomes included oocytes retrieved, metaphase II(MII)oocytes and ovarian sensitivity index(OSI), the latter defined as:(number of retrieved oocytes/total gonadotrophin dose)×1000.

Main results and the role of chance: 113/471 cases with endometriosis and concomitant autoimmunity and 358/471 age-matched endometriosis only controls were enrolled. The mean age was 35.70±3.75 and 35.95±3.72 ($p = 0.543$) in cases and controls respectively. No baseline differences in endometriosis disease stage ($p = 0.414$), surgical treatment for endometriosis prior to IVF ($p = 0.617$), BMI ($p = 0.866$) or type of infertility ($p = 0.255$) were observed when comparing the two groups. In "expected normo-responders", cases with autoimmunity had significantly higher numbers of oocytes retrieved ($p = 0.007$), MII oocytes ($p = 0.007$) and OSI index ($p = 0.013$) when compared to controls with endometriosis only; the CPR was 12.5% in cases vs. 17.5% in controls, thus comparable between the two groups ($p = 0.143$). In "expected poor-responders" no significant differences were observed neither in the number of oocytes retrieved and MII oocytes, nor in OSI index; the CPR was 12% in cases with concomitant autoimmunity compared to 7.75% in controls with endometriosis only ($p = 0.256$). In the generalized linear models (GLMs) of independent predictors associated with CPR, in expected 'normo-responders' autoimmunity was the only significant negative predictor of CPR ($p = 0.004$) whereas in 'poor-responders' only age negatively affected CPR ($p = 0.001$).

Limitations, reasons for caution: This study has a retrospective design. The interpretation of results is based on the validated yet still debated definition of poor-responders according to Bologna Criteria. Results should be interpreted with caution until replicated by future research providing multicentric and prospective design, larger sample size and more standardized data collection.

Wider implications of the findings: Autoimmunity does not seem to impact neither ovarian reserve nor ovarian response to gonadotropin, as it may act a 'competitive' rather than 'additive' risk factor for infertility in endometriosis. However, in 'normo-responders' autoimmunity seems to reduce the chances of pregnancy following IVF/ICSI perhaps impairing endometrial receptivity and embryo implantation.

Trial registration number: Due to the retrospective design of the study, full IRB approval at the institution was not needed.