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The 15th Editorials

Do severe endometriosis-related painful symptoms impact assisted reproductive technology (ART) live birth rates?

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What is known already?

ART is currently recognized as one of the main therapeutic options for managing endometriosis-associated infertility. It is generally resulting in satisfactory outcomes [1] (Maignien et al., 2017; [2] Quet al., 2022).

However, there is still much to discover regarding the impact of the disease on ART outcomes to help individualize the therapeutic management of infertile endometriosis patients [3] (Becker et al., 2022).

An interesting but still unaddressed issue in this field is whether intense pain symptoms are associated with altered ART outcomes?.

Endometriosis-associated pain appears to originate to a large extent from chronic inflammatory processes [4] (Gruber and Mechsner, 2021), with a correlation between the intensity of pain symptoms and the extent of the inflammatory response[5] (Santulli et al., 2012; [6] Gibson et al., 2021)

It was hypothesized that inflammation could negatively impact oocyte quality and/or endometrial receptivity [7] (de Ziegler et al., 2010a; [8] Bonavina and Taylor, 2022)

To date, scant attention has been paid to the association between pain, which is the key symptom of the disease, and ART results.

The few available studies regarding pain symptoms and ART aimed at analyzing pain evolution during ovarian stimulation, to assess the impact of ART on endometriosis progression [9 (Benaglia et al., 2011; [10] Santulli et al., 2016a; [11] Mathiasen et al., 2019)

What is New?

In a recent observational cohort study of 354 endometriosis patients, who underwent 711 ART cycles was conducted at a tertiary care university hospital [12]

In this study, diagnosis of endometriosis was based on published imaging criteria using transvaginal sonography, magnetic resonance imaging, and histologically confirmed in women who had a previous history of endometriosis surgery (n=127, 35.9%).

The intensity of the painful symptoms due to noncyclic chronic pelvic pain, gastrointestinal pain or lower urinary tract pain was evaluated using a 10-point visual analog scale Howard, 2003; Fauconnier et al.,2009), where, severe pain was defined as having a pain score of $\geq$7 for at least one pelvic pain symptom (Santulli et al., 2016a; Allaire et al., 2018; Bourdon et al., 2023).

This study reported that:

1- The mean visual analog scale scores for dysmenorrhea, dyspareunia, and GI pain symptoms were 6.6 $\pm$ 2.7, 3.4 $\pm$ 3.1, and 3.1 $\pm$ 3.6, respectively.
2- A 242 patients (68.4%) had severe pain symptoms. The CLBR per patient was 63.8% (226/354).
3- Neither the mean visual analog scale scores for the various painful symptoms nor the proportion of patients displaying severe pain

differed significantly between patients who had a live birth and those who had not, based on univariate and multivariate analyses (P¼0.229).

4- The only significant factors associated with negative ART live births were age >35 years (P<0.001) and anti-Müllerian hormone levels<1.2 ng/ml (P<0.001).

Clinical Implications

Rather than considering a single argument such as severe pain, the decision-making process for choosing between ART and surgery in infertile endometriosis patients should be based on a multitude of aspects, including:

1. The patient's choice.
2. The associated infertility factors.
3. The endometriosis phenotypes.
4. The efficiency of medical therapies in regard to pain symptoms, through an individualized approach guided by a multidisciplinary team of experts.

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